THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 8 — CHICAGO, ILLINOIS — JUNE 21, 1958

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958
167

ELECTROENCEPHALOGRAPHIC STUDY OF PERSONS BEFORE AND AFTER POLIOMYELITIS VACCINATION

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Electroencephalograms were obtained from 852 normal subjects before and after the first, second, and third inoculations with Salk vaccine for poliomyelitis. The series included infants, children, adolescents, and adults. No electroencephalographic abnormalities were induced by the vaccination in initially normal people. The possibility that vaccination might cause detectable injury in brains already handicapped by previous disease or injury was also investigated. A group of 106 persons with brain disorders, including 44 with epilepsy, were studied electroencephalographically. Again no evidence of harm from the vaccination was obtained. The vaccines used in this study were commercial preparations from two drug companies, and the evidence showed that these preparations could be given safely to patients with or without manifestations of preexisting cerebral disease.

In 1956, shortly after a program of mass vaccination for poliomyelitis with Salk vaccine was started in the Chicago area, reports began to circulate of children who had developed convulsions or other signs of central nervous system disorder supposedly as a consequence of vaccination. One of the first cases to come to our attention was that of a 14-year-old boy who became seriously ill two days after receiving his second injection of Salk vaccine. His condition deteriorated rapidly and ended in death. The report of this spread rapidly through the community. The full clinical history, however, revealed that the patient had had enuresis since birth. He had had chronic pyelonephritis with severe hypertension and extensive encephalopathy. He developed a severe pain in the left flank the day before the second Salk vaccination. The postmortem diagnosis was pyelonephritis with overwhelming sepsis and uremia. It seemed unlikely, in this case, that the Salk vaccination was causally related to the final illness.

To track down every patient who develops convulsions or other symptoms as an apparent untoward reaction to Salk vaccine in order to determine whether or not the vaccination was actually the cause would be difficult or impossible. Seizures of various types are so common in children that cases are certain to be encountered where the time relationship between the first epileptic seizure and the Salk vaccination would make the vaccination a "reasonable presumptive cause." Sudden inexplic-

able illnesses, some of which defy even the most expert diagnosticians, occur in a large number of children. By coincidence, an unexplained illness could follow a Salk vaccination at just the right time to convince the family and even the physician in charge that the vaccination was responsible for the child's illness or even his death.

TABLE 1.—*Electroencephalographic Study of 852 Persons Receiving Salk Vaccine*

Age, Yr.	Recordings Before and After Injection, No. 1st	2nd	3rd	EEG Change
<1	32	32	20	-
1-2	52	52	70	-
3-5	110	110	182	1
6-10	53	53	183	-
11-15	120	120	197	-
16-19	81	81	81	-
20+	121	121	119	-
Total.....	569	569	852	

Does Salk vaccine, when administered as part of a program of mass immunization against poliomyelitis, cause brain disorder in some persons? This question seemed worth answering. The electroencephalogram is a sensitive indicator of acute encephalitic types of reaction. A great variety of viruses produce abnormal slow activity in the electroencephalogram during the acute and immediate postacute stages of virus infections, even when no clinical evidence of encephalitis is present.[1] Vaccines of various types, for example, rabies and also the triple vaccine of whooping cough, diphtheria, and tetanus, can produce brain disorder and, with it, definite electroencephalographic abnormalities.[2] It seemed desirable to proceed with a controlled encephalographic study of patients receiving Salk vaccine.

Material and Method

Arrangements were made to obtain electroencephalograms of infants, children, adolescents, and adults before and after the first, second, and third inoculations with Salk vaccine. Commercial preparations from two drug companies were used. In each vaccination, 1 cc. of Salk vaccine was given intramuscularly. To guard against the possibility of preexisting electroencephalographic abnormality going unrecognized, to be picked up after vaccination, we carried out careful preliminary electroencephalographic study on all patients. Recordings were made with patients in the waking and the sleeping states with leads in the frontal, parietal, temporal, and occipital areas on both sides. Recordings were made 24 hours after the vaccination in three-fourths of the patients and 48 hours after the vaccination in one-fourth. In a few cases recordings were made at daily intervals for four days after vaccination.

The number of normal subjects obtained in each age group and the number of recordings before and after the first, second, and third inoculations are indicated in table 1. A group of patients with epilepsy and/or brain damage was also studied, because it seemed possible that such persons might be more sensitive to Salk vaccine than persons with normal brains; the age distribution of this group is shown in table 2.

Some difficulty was encountered in finding 2-to-5-year-old children in the Chicago area who had not received first and second vaccinations. This is a tribute to the thoroughness of the mass vaccination program in the years 1956 and 1957. We discovered that children who had not already been vaccinated usually came from families with a general prejudice against scientific medicine and a particular prejudice against medical research. Although electroencephalographic studies are not painful, the need for them in the present instance was hard to explain without arousing suspicion or alarm. The troublesomeness of six visits for the before-and-after electroencephalograms, as compared with only three visits for the usual Salk vaccination, was a powerful deterrent to parents and subjects.

Stations for electroencephalographic studies were set up in the following hospitals: Chicago Municipal Contagious Hospital, Cook County Hospital, Illinois Neuropsychiatric Institute, and Rockford Memorial Hospital. The Morton High School and the Nazareth Academy installed temporary electroencephalographic laboratories for this study. A station was also set up in the office of Dr. John Kendrick in Richmond, Va. The recordings from the Rockford and Richmond areas were used to check on the possibility that local conditions, for example, the recent poliomyelitis epidemic in Chicago (1956), might affect the results.

Results

In only one case, considered in detail in a later paragraph, was the electroencephalogram significantly altered. This is astonishing. We had not expected to obtain such completely negative results with a biologically potent material. One child with cerebral palsy died of pneumonia (unrelated to vaccination) after the second inoculation. Two children with brain disorder moved out of Chicago before the third inoculation.

TABLE 2.—*Electroencephalographic Study of 106 Persons with Brain Disorder Receiving Salk Vaccine in Whom No Electroencephalographic Change Was Observed**

Age, Yr.	Recordings Before and After Injections 1st	2nd	3rd
<1	9	9	9
0-2	30	30	29
3-5	25	25	23
6-10	20	20	20
11-15	13	13	13
16-10	1	1	1
20+	8	8	8
Total.....	106	106	103

* 44 with epilepsy; 24 with cerebral palsy; 38 with other disorders.

In two cases we received alarming reports that the child had developed clinical symptoms which prevented his return for the postvaccination re-

cording. On checking up on these two cases, however, we found that in one case the child was entirely well and his mother had only wished to avoid the trouble of bringing him in for further study. In the other case, the mother mistook the symptoms of an uncomplicated upper respiratory infection for a postvaccination reaction.

One child, 5 years of age, developed slow waves in his electroencephalogram 24 hours after his third shot. It was feared that this might be a reaction to the vaccine. He had a fever at the time of the recording, and in the next five days he went through the typical course of an attack of Asiatic influenza. His symptoms were identical with those of the other members of his family who also contracted this disease. We saw numerous patients with an encephalitic type of reaction to Asiatic influenza. Usually in these cases the slow activity is transitory; this child's electroencephalogram normalized within a few days. However, the experience made us decide not to complicate our study by continuing Salk vaccinations during the epidemic of Asiatic influenza.

Summary and Conclusions

Electroencephalographic study of 852 normal infants, children, adolescents, and adults indicates that Salk poliomyelitis vaccine produces no electroencephalographic abnormalities. This gives assurance that Salk vaccine is unlikely to cause an encephalitic type of reaction or brain injury. Electroencephalographic study of 106 patients with epilepsy and with brain damage indicates that such patients can be safely given Salk vaccine.

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This study was aided, in part, by a grant from the National Foundation for Infantile Paralysis.

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958
167

INTRACRANIAL ANEURYSM IN THE GERIATRIC PATIENT

REPORT OF THREE SURGICALLY TREATED PATIENTS

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One of the most common stigmata of aging is the occurrence of vascular degenerative changes which are often most pronounced in the intracranial blood vessels. Incident to these vascular degenerative changes, secondary pathological changes may develop, such as arteriosclerotic intracranial aneurysm.[1] Since there is a progressive increase in the number of patients entering the geriatric span of life,[2] it would seem logical to expect a corresponding increase in the number of patients with such intracranial aneurysms. A perusal of the available literature does not reveal a wide surgical experience in the management of this particular type of aneurysm (arteriosclerotic) in this particular age group. We therefore thought it of interest to report our surgical experience in the management of three cases of proved intracranial aneurysm developing in patients in the seventh and eighth decades of life.

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Intracranial aneurysms were demonstrated in three patients, aged 66, 76, and 77. Because of the unendurable pain and advancing neurological deficits surgical intervention became mandatory. The authors present the details of their surgical management of these cases. The article serves to emphasize the occurrence of intracranial aneurysms in the geriatric patient and the possibility that such vascular lesions may become more frequent in an aging population.

Report of Cases

CASE 1.—A 66-year-old woman was examined because of the complaints of headache, nausea, and vomiting. The medical history was negative with the exception of "pneumonia" two years previously. The patient was alert and oriented. The blood pressure was 146/68 mm. Hg; pulse rate, 84 per

minute; and respiratory rate, 24 per minute. There was ptosis of the right eyelid (fig. 1), and hyperesthesia to pinprick over the supraorbital and maxillary areas on the right. The neurological examination was otherwise normal. X-rays of the skull and chest were normal. Urinalysis showed a trace of albumin but was otherwise negative. The hemoglobin level was 9.9 Gm. per 100 cc. The hematocrit was 32%. The blood urea nitrogen level was 20 mg. per 100 cc. The fasting blood sugar level was 131 mg. per 100 cc. The serologic tests were negative.

Fig. 1 (case 1).—Ptosis of right eyelid.

A diagnosis of intracranial aneurysm was made. A right cerebral arteriogram was done under thiopental (Pentothal) anesthesia, percutaneously, using 50% diatrizoate (Hypaque) as the contrast medium. A large aneurysm of the right internal carotid artery was demonstrated (fig. 2). Four days after angiography, the patient was taken to surgery where the right common carotid artery was exposed. A Poppen-Blalock arterial clamp was placed about the vessel. After preliminary stellate ganglion procaine (Novocain) block and periarterial procaine irrigation, the clamp was tightened to produce about 50% occlusion of the arterial lumen. The patient tolerated the procedure without difficulty. The patient was returned to the ward and placed in a cooled oxygen tent. In addition, she was given regular intramuscular doses of papaverine and large doses of vitamin B complex.

Twenty-four hours later the clamp was tightened to reduce further the remaining volume of carotid blood flow. The patient tolerated this without incident. Seventy-two hours after placement, the clamp was closed to produce total arterial occlusion. No neurological deficits developed. Three days later the patient was returned to surgery where double chromic ligatures were placed about the common carotid artery both above and below the point of clamp occlusion. The arterial clamp was then removed. The patient was discharged from the hospital 10 days later free of pain but with ptosis of the right eyelid. The patient has remained pain free. Since her discharge there has been complete recovery from ptosis of the eyelid (fig. 3).

Case 2.—A 77-year-old woman was admitted to the neurosurgical service because of persistent left-sided headache of insidious onset about six months prior to admission. Since that time the pain had persisted and had not responded to symptomatic therapy. The patient was currently receiving treatment for hypertension and cardiac decompensation. The medical history was negative except for bilateral simple mammectomy in 1910 for "cystic disease of the breasts."

The patient was alert and oriented. The blood pressure was 190/110 mm. Hg; pulse rate, 100 per minute; respiratory rate, 20 per minute. There was an incomplete ptosis of the left eyelid; the neurological examination was otherwise normal. X-rays of the skull were normal. The chest plate showed a moderate cardiac enlargement with minimal aortic calcification. The hemogram was normal. The urinalysis was normal except for a "slight trace" of albumin. The blood urea nitrogen level was 20 mg. per 100 cc. The fasting blood sugar level was 118 mg. per 100 cc. The serologic test was negative. An electrocardiogram was interpreted as showing left axis deviation with evidence of myocardial change.

A diagnosis of intracranial aneurysm was made. Clinically the patient was a poor risk for any surgical procedure. However, her head pain was of such an unbearable nature that she requested some effort be made to give her relief, although the dangers of any such procedures were understood. Accordingly, a left carotid cerebral arteriogram was done, percutaneously, under thiopental anesthesia, using 50% diatrizoate as the contrast medium. A large intracranial aneurysm was outlined arising from the left internal carotid artery. Four days after arteriography, the patient was taken to surgery where the left common carotid artery was exposed. After procaine block of the stellate ganglion and peri-

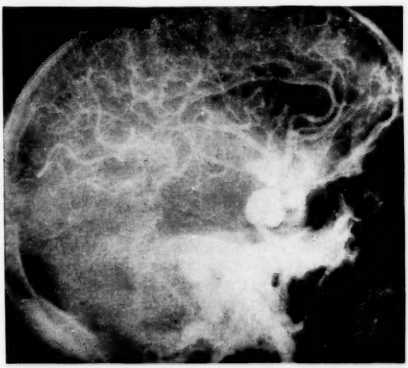

Fig. 2 (case 1).—Right cerebral arteriogram demonstrating aneurysm of right internal carotid artery.

arterial procaine irrigation, a Poppen-Blalock clamp was placed about the artery and closed to produce about 50% arterial occlusion. The patient tolerated the procedure without difficulty. She was returned to the ward where treatment included high concentration of cooled oxygen per tent. In addition, she was given papaverine parenterally and large doses of vitamin B supplement.

Twenty-four hours later the Poppen-Blalock clamp was tightened to occlude about one-half of the remaining arterial lumen. No neurological deficits developed. The following day the arterial clamp was completely closed. Two hours after this the patient "fainted" and developed hemiparesis on the right side. These were transient changes and the patient reportedly rapidly recovered consciousness with no obvious motor weakness. No report was made of this incident by those in immediate attendance. Eight hours later the patient abruptly developed a total aphasia and hemiplegia on the right side. The arterial clamp was immediately fully opened.

Fig. 3 (case 1).—Recovery from ptosis of right eyelid postoperatively.

In spite of this, the hemiparesis and aphasia persisted and the conscious level deteriorated. The stupor persisted. The patient died 30 days after total arterial occlusion. No autopsy was permitted.

Case 3.—A 76-year-old male was admitted to the neurosurgical service because of "sticking pains" behind the left eye and a "droop" of the left eyelid. The patient first experienced a sudden, severe, left retro-orbital pain about two months prior to admission. Thereafter he noticed his "left eye began to droop." Three days after onset of pain, the ptosis was complete. The pain persisted. The patient was a known diabetic of 15 years' duration. He required no insulin therapy but was controlled by dietary measures. Five years prior to this examination he had a transurethral resection for benign prostatic hypertrophy.

The patient was alert and well oriented. The blood pressure was 150/70 mm. Hg; pulse rate, 72 per minute. There was a complete ptosis of the left eyelid (fig. 4). The left pupil was dilated and there was lateral deviation of the left eye. There was loss of upward, downward, and inward ocular movements on the left. The neurological examination was otherwise normal. The x-rays of the skull and chest were normal. The hemogram was normal. The urinalysis showed no abnormalities. The blood urea nitrogen level was 23 mg. per 100 cc. The fasting blood sugar level was 83 mg. per 100 cc. The serologic test was negative. A diagnosis of intracranial aneurysm was made. A left carotid cerebral arteriogram was done, percutaneously, with the patient under thiopental anesthesia, with use of 50% diatrizoate solution as the contrast medium. A large aneurysm arising from the left internal carotid artery was demonstrated (fig. 5).

Three days after arteriography, the patient was taken to surgery where the left common carotid artery was exposed. After procaine block of the left stellate ganglion and procaine irrigation of the periarterial tissue, a Poppen-Blalock clamp was placed about the artery, then tightened to produce about 50% occlusion of the arterial lumen. The patient tolerated the procedure without difficulty. Postoperatively, his treatment included the use of high concentrations of cooled oxygen per tent. In addition, the patient was given papaverine intramuscularly and large doses of vitamin B supplement. Twenty-four hours later the clamp was tightened to further reduce carotid blood flow.

The next day the clamp was completely closed. No neurological deficits developed. Twenty-four hours later the patient was returned to surgery, where double chromic sutures were placed about the common carotid artery both proximal and distal to the point of clamp occlusion. The patient tolerated the procedure without incident. He was discharged from the hospital free of pain five days after

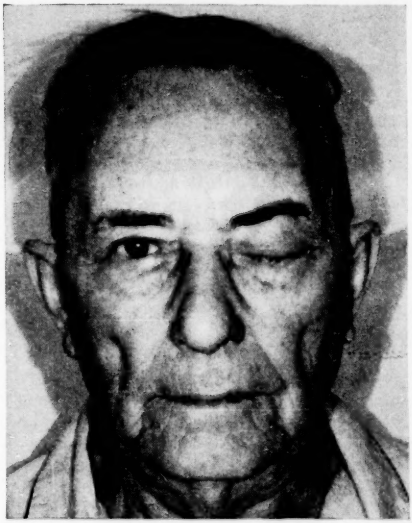

Fig. 4 (case 3).—Complete ptosis of left eyelid.

ligation. The oculomotor paresis persisted. Since discharge, the patient has remained free of pain. There has been excellent return of oculomotor nerve function (fig. 6).

Comment

Three patients with intracranial aneurysm were respectively 66, 77, and 78 years of age. McDonald and Korb,[3] in culling the world's literature, found

only 41 authenticated cases of intracranial aneurysm in people over 70 years of age. Later Dandy in his series [4] reported only seven patients beyond the age of 70 years. Other series [5] have listed a total of 200 cases of proved intracranial aneurysm

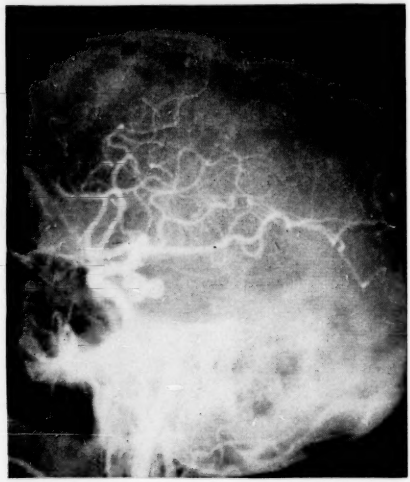

Fig. 5 (case 3). Left cerebral arteriogram demonstrating aneurysm of left internal carotid artery.

with but one patient beyond the 70th year of age. In these reports only 14 patients were listed in the 60-through-70-year age group.

Other studies have shown that atherosclerotic vascular lesions are not uncommon at the site of origin of arteriosclerotic aneurysms.[2] As the individual lives to an older age with accompanying vascular changes, aneurysms of this origin may become more frequent. If the catastrophe of subarachnoid hemorrhage resulting from rupture of such aneurysms is to be avoided, the existence of the lesions must be suspected. The cases reported here may serve to focus attention on the occurrence of intracranial aneurysms in elderly patients.

In cases of suspected intracranial aneurysm, cerebral angiography is required to establish the diagnosis. The employment of the percutaneous carotid puncture, under thiopental anesthesia, and the use of 50% diatrizoate solution as the contrast medium [6] has reduced the trauma of this procedure to a minimum. Using these techniques, we do not consider advanced age, per se, as a contraindication to cerebral angiography.

The management of the elderly patient with a proved intracranial aneurysm presents a particular surgical challenge. The question of ligation of the carotid artery in the aged individual has been a focal point of controversy. On the one hand there have been those such as Dandy [7] and Cushing [8] who believed that in persons over 45 years of age, ligation of the internal carotid artery becomes increasingly hazardous. On the other hand, the reports of Pilcher and Thuss [9] among others described no increase in the incidence of complications after carotid ligation in elderly patients.

Our experience indicates that carotid ligation may be successfully employed in the treatment of aged patients with intracranial aneurysm. In our cases 1 and 3, the patient was completely free of pain and regained oculomotor nerve function after treatment by common carotid artery ligation on the involved side. In each case the Poppen-Blalock clamp was used for controlled carotid occlusion.

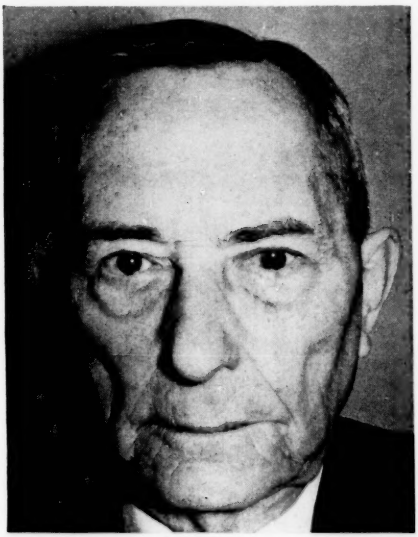

Fig. 6 (case 3).—Recovery of oculomotor nerve function postoperatively.

During the course of carotid occlusion, supplemental therapy included the use of high concentrations of cooled oxygen, liberal amounts of vitamin B, glucose parenterally and papaverine intramuscularly. Where indicated, whole blood transfusions were judiciously used to increase the oxygen-carrying ca-

pacity of the blood. We believe that these adjuncts are important in the successful clinical management of such patients.

Recently Bassett and co-workers [10] have questioned the advisability of any form of surgical treatment in the elderly patient with intracranial aneurysm. These authors stated that "Not all angiographically verified aneurysms are amenable to surgical treatment; those encountered in elderly patients with advanced arteriosclerosis and hypertension are better left alone." We believe that in geriatric patients with advancing neurological deficits, or in instances where pain arising from these lesions makes life unbearable (case 2), surgical intervention may become mandatory.

Recently, Gurdjian and Webster [11] reported studies emphasizing the value of preligation carotid compression tolerance tests. These procedures may prove of value in averting some of the circulatory sequelae that may follow carotid ligation. Our single failure may have been averted if the significance of the "fainting spell" had been appreciated by those in immediate attendance, so that full carotid flow could have been immediately reestablished.

On the basis of our experience of an admittedly small group of patients, it appears that staged occlusion of the common carotid artery is useful in the surgical management of intracranial aneurysm in the aged patient. Although the advantages of direct surgical attack are understood, the narrowed physiological reserves of the elderly patient may preclude the use of this surgical approach.

The question of the most desirable anatomic level for arterial ligation in the neck has been studied.[12] The comparative value of internal carotid ligation versus common carotid artery ligation in the management of intracranial aneurysm is still moot. However, in a recent report, Davis and associates [13] concluded that there was little difference therapeutically between internal carotid and common carotid ligation in the surgical treatment of intracranial aneurysm.

The effect of rate of arterial occlusion on the carotid system hemodynamics has been studied.[14] There is conflict of opinion regarding the physiological advantages of graded arterial occlusion. Based on our experience, however, we feel that the use of the clamp technique allows for controlled occlusion of the involved artery and a means for immediate reestablishment of carotid flow if clinically required. Further investigation of this problem of surgical management of cerebral aneurysm in the aged patient is indicated.

Summary

In three cases of intracranial aneurysms occurring in the geriatric age patient, the surgical treatment consisted of staged occlusion of the common carotid artery, with successful experience in two of the three cases. Such lesions will in all probability be encountered more frequently.

100 N. Euclid (8) (Dr. Smolik).

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CHALLENGE OF FETAL LOSS, PREMATURITY, AND INFANT MORTALITY—ASSESSING THE LOCAL SITUATION

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A concerted study by various agencies in New York City in 1933 started a campaign to reduce maternal mortality. The goal initially set was ultimately surpassed; by 1945 the mortality had fallen below the previously assumed minimum of 17 per 10,000 live births. Nevertheless the cause of maternal death is still in many instances recognized as a preventable one. Infant mortality likewise has been greatly reduced by comparison with the appalling figures for 1915, but recent progress in reducing neonatal deaths, particularly deaths in the first week of life, has been slight. The highest mortality rates in New York, for mothers and infants alike, are from districts with poor socioeconomic status. Within given categories of hospitals influenced by population composition a range of perinatal mortality is exhibited. The program for improving the care of premature infants has saved many lives, but postneonatal morbidity is still serious and the postneonatal mortality for prematurely born infants has not declined appreciably. The mechanisms that precipitate early labor are not entirely understood, and common sense demands an enlarged, coordinated research attack on these fundamental problems. Serious problems also exist in hospitals, especially due to the shortage of staff members. Prenatal clinics must be improved. Better teamwork among physicians and ancillary workers is needed in the maternity services, and more extensive facilities and additional nurses are needed for the care of the prematurely born infant. Continuing special attention must be given to the emergency problems created by the immigration of so many underprivileged people into the city. The ideal should be to give economically underprivileged babies the same chance for life and health that other babies have.

For too long a time, late fetal and early neonatal deaths have been considered separately. However, the deaths that occur just before, during, and just after the process of birth are all associated with the same biological process. It obviously makes great sense to look at them as an entity. The newer concept of "perinatal mortality" is therefore a useful and important one.

The term "perinatal mortality" is used somewhat differently by different persons, but this fact is not of great importance. The word "peri" means "around." In using it, some go back a little further from the moment of birth, others go forward a little further. The important fact is that all the deaths associated with the child-bearing process are here viewed simultaneously.

New York City figures are of interest, for they have a certain degree of accuracy not always obtainable in studies involving a total population in a community. For many years the Health Department has worked closely with the medical societies, hospitals, and physicians in the city. Together they have worked out a system of reporting a great deal of information concerning the medical condition of the mother and child at the time of birth and death in a confidential medical report which is attached to birth and death certificates. These reports are used only for statistical and scientific purposes. Reporting is unusually complete, and, although the material on the certificates is certainly not as accurate as that obtained by firsthand review of clinical records or contemporary scientific study, yet many of the errors are unquestionably compensated for by the large numbers involved.

The observations to follow are based on analyses made of the materials reported by physicians in these confidential medical reports of all births in New York City. The methods used for obtaining mortality rates are shown at the foot of each table. Such data, based on a total population in a community of 8 million persons, lend themselves to certain analyses not possible with data from smaller or more selected groups, such as patients in hospitals or members of group insurance plans.

In 1955, in New York City, 165,150 babies were born. Of these, 4,268 died before reaching their first birthday, and of these deaths more than two-thirds (2,921) occurred in the first week of life. Coupled with the loss of liveborn infants was the loss of viable fetuses of 28 weeks' gestation and over.

From the New York City Department of Health.
Read in part before the Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

These fetal deaths amounted to 2,233 in 1955. These two groups of deaths (totaling 5,154) will be considered together as an entity with the descriptive designation of "perinatal" mortality. Numerically the perinatal deaths (5,154) constitute a larger group than fatalities due to accidents (3,034), tuberculosis (1,084), or diabetes (1,698). The reduction of perinatal mortality quite properly is, therefore, a challenge, and the time has certainly come for a consolidated attack on the problem of reducing the loss of life in this period.

Maternal Mortality

Since the health of the mother is important to the survival of the infant, the facts concerning maternal mortality are briefly presented. In 1915, for every 200 live births a mother's life was lost. Maternal deaths continued at this high rate for the next 20 years. It was not until after a concerted interest in the problem was aroused in 1932 and a program for curbing maternal deaths was begun that rates began to fall. In these years, the New York Academy of Medicine, in cooperation with certain voluntary agencies and the Health Department, undertook a study of maternal deaths.[1] It was concluded that two-thirds of maternal deaths were preventable and that, therefore, a reduction to 17 deaths per 10,000 live births would be an irreducible minimum. Maternal mortality committees which are still active were set up in each county of the city to review and investigate all maternal deaths with the aim of eliminating avoidable and unnecessary deaths. Obviously, better obstetrics, wider use of blood transfusions, and the discovery of antibiotics all played a role in the decline in maternal mortality which followed.

By 1945 the so-called irreducible minimum had been reached; only 17 mothers for every 10,000 live births were lost. Within a decade (1955) the rate dropped to 5 per 10,000, representing a 70% decrease below this irreducible minimum. It is reasonable to believe that even now the minimum has not been reached, since the cause of death is still in many instances a preventable one. It must be reemphasized that the mortality or condition of the mother is closely linked to the baby's survival too.

Infant and Fetal Mortality

Infant Mortality.—Again glancing back to the year 1915, we see an appalling loss of babies in the first year of life—for every 10 babies born alive then, 1 would die. Many of these deaths were needless, particularly those due to diarrhea and infection. These causes of death have largely been eliminated, with a resultant decrease in infant deaths postneonatally, i. e., after the first month of life. The cooperative efforts of doctors, health officials, and public-spirited citizens, resulting in a safe milk supply, improved sanitation, and education of the public in the fundamentals of hygiene and baby care, as well as the improved medical care of sick infants, were responsible for continuing improvements.

But there is little cause for complacency. From 1945 to 1955 the infant mortality rate in New York City dropped only 16%, from a rate of 31 per 1,000 live births to 25.8, and, as is readily seen in figure 1, has tended to level off. Maternal mortality in this same period dropped 70%.

Infant deaths viewed according to age at death may be divided into two groups—deaths of infants in the neonatal period (under 28 days) and those in the postneonatal period (28 days to one year). Deaths in the neonatal period now comprise three-fourths of all infant deaths, and of these neonatal deaths 90% occur in the first week of life (fig. 2). Approximately four-fifths of the deaths in the first week of life are due to causes associated with birth itself, namely, immaturity, 37%, anoxia and conditions of abnormal pulmonary ventilation, 26%, and birth injuries, 10% (fig. 3). Progress in reducing

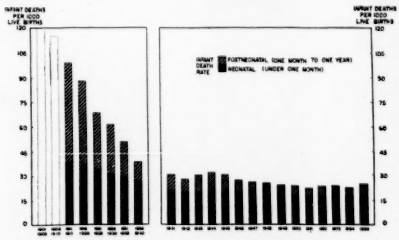

Fig. 1.—Infant mortality rate in New York City, 1901-1955 (neonatal data not available prior to 1911).

neonatal deaths, particularly those occurring in the first week of life, has been slight. As is well recognized, the reduction of infant mortality is due to gains made in saving the lives of those who live at least one month.

Fetal Mortality.—It is helpful to break down fetal deaths into three groups, depending on length of gestation, i. e., 28 weeks and over, 20 through 27 weeks, and under 20 weeks. The first two groups, i. e., late and intermediate fetal deaths, are quite completely reported in New York City. For the six years from 1949 through 1954, deaths of fetuses of 28 weeks' gestation and over decreased from 16.4 per 1,000 live births to 14.1 per 1,000—a drop of 14%. In the group of combined late and intermediate fetal deaths, those at 20 weeks' gestation and over, the reduction was only 8% (from 25.2 per 1,000 live births to 23.0 per 1,000 live births). For deaths of fetuses of under 20 weeks' gestation, we have noted a rapid rise in the ratio through the years. Better and more accurate reporting of deaths in this group undoubtedly accounts for this increase. Even now, reporting of fetal deaths is far

from complete in this group of early fetal deaths.[2] In 1955, the total fetal death ratio was 123 for every 1,000 live births. The losses associated with deaths of viable and previable fetuses thus represent an enormous wastage of life.

Perinatal Mortality

As pointed out earlier, it is important to consider all the deaths closely associated with birth as a unit. Perinatal mortality, as routinely defined in New York City, is the combination of late fetal deaths (gestation of 28 weeks and over) and deaths occurring at time of delivery and in the first seven days of life. (The perinatal mortality rate is determined by multiplying this sum by 1,000 and dividing by total live births plus fetal deaths.)

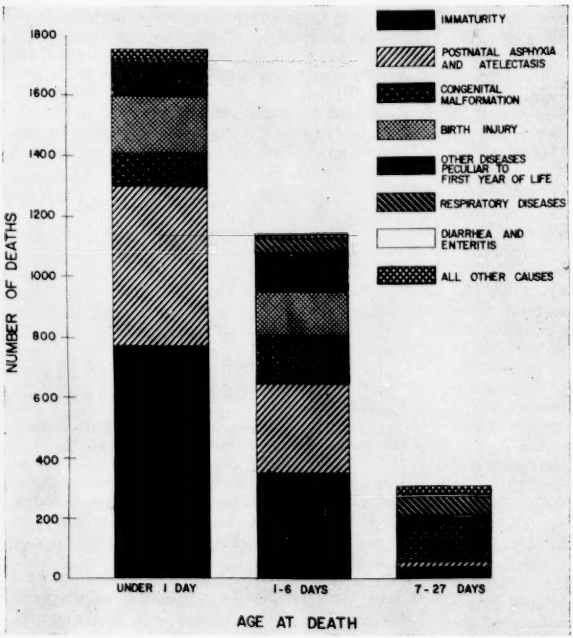

Fig. 2.—Neonatal mortality, by age and cause of death, in New York City, 1955.

Since 1949, progress in reducing perinatal deaths has been slow. There are slight variations from year to year. The perinatal mortality rates showed an 8.5% decrease from 32.6 in 1949 to 29.8 in 1954. However, in 1955 it rose again to 30.8 (table 1). In this same year, a rise occurred both in the neonatal and postneonatal periods for both white and nonwhite groups. These rises were statistically significant compared with the previous year, with the infant death rate rising from 23.7 to 25.8 and the neonatal mortality rate from 18 to 19.8. In the same year, 1955, the incidence of prematurity also showed a statistically significant rise from 8.8% to 9.4%. On the other hand, the late fetal deaths or stillbirth rate exhibited a slight decrease. This might mean that more of these fetuses were born alive and were augmenting the ranks of the prematurely born, poor-risk babies dying in the first week of life. This phenomenon one of us and a co-worker pointed out many years ago.[3] The average perinatal death rate for 1949 through 1955 is 30.6 (fig. 4). In short, there has not been great progress in curbing deaths associated with childbearing in the past five years.

A striking correlation exists between high incidence of prematurity, high perinatal death rates, and high incidence of late and no prenatal care. These, in turn, are associated with socioeconomic factors. Hospitals caring mainly for the lower socioeconomic groups had a high incidence of prematurity and a high perinatal death rate.[4] Conversely, hospitals catering only to private patients had a comparatively low incidence of prematurity and a low perinatal death rate (fig. 5). Furthermore, out-of-wedlock births are associated with higher fetal and infant death rates, higher incidence of prematurity, and higher incidence of late or no prenatal care. Out-of-wedlock births appear to be on the increase in the city and have been estimated conservately at 5.5% of all births.

The past five years in New York City have witnessed sustained high birth rates as well as population shifts. Since 1951, increasing proportions of births have occurred in nonwhite and in Puerto Rican groups and a decreasing proportion in white groups other than Puerto Rican. Births were 8% fewer in white groups (exclusive of Puerto Rican) but 15% more in nonwhite and 73% more in Puerto Rican groups (table 2). Since the nonwhite and Puerto Rican population in New York City is to a great extent confined to the lower socioeconomic groups, it is not surprising that a higher incidence of prematurity and higher perinatal death rates are found among these groups. In 1955, 165,150 births occurred, with a noticeable increase in general service cases from 32.3% in 1951 to 35.7% in 1955 (fig. 6). A higher incidence of deliveries was noted also

for women receiving late or no prenatal care, with a rise in this group from 10.6% in 1951 to 15.6% in 1955.

The relationship of the socioeconomic factors to perinatal mortality can be demonstrated in other ways. For administrative purposes, New York City is divided into 30 health districts and each, in turn, is divided into health areas. A wide variation exists among these in incidence of prematurity, percentage of deliveries to women receiving late or no prenatal care, and fetal and infant death rates. The correlations are quite consistent. The districts heavily weighted with a lower socioeconomic population have the high mortality rates. The wide differences which exist are seen in table 3, and districts are further compared in table 4. In terms of preventable deaths, for 1955 alone it is estimated that 1,745 babies additionally could have lived if the rate of the most favorable district had prevailed city-wide. This is a conservative estimate, for preventable fetal deaths are not included.

The municipal hospitals which care for the lowest socioeconomic groups have the highest perinatal rates, 49.3, while the proprietary hospitals, caring only for private, paying patients, show the lowest perinatal rates, 22.6 (fig. 5). The quality of care in a given hospital cannot be judged solely by its perinatal mortality rate, which appears to be greatly influenced by the socioeconomic level of the population served. For this reason, we are presently grouping hospitals according to the type of patient cared for. Within a given category of hospital, a range of perinatal mortality is exhibited. It is only then that comparisons with a degree of validity can be drawn.[4] The size of the hospital may also influence the degree of variation in a rate—a small hospital obviously may experience a fluctuation in rate which may not be statistically significant because of small numbers, while the same fluctuation in a large hospital service may well be statistically significant. Since 1949, the perinatal rates in each category of hospital have shown a slight downward trend.

One can obviously view these data concerning perinatal mortality from the point of view of population changes. The failure to reduce infant mortality may then be attributed in New York City to changes in population composition, as we have shown, for there are greater proportions of births in these groups associated with higher mortality. However, that is not the real issue. To prevent mortality and morbidity in the less-favored socioeconomic groups is the real challenge. What else do we know of these losses? What has been done to curb them? What needs to be done?

Prematurity

The definition of prematurity used is that established by the World Health Organization in 1948, i. e., a weight at birth of 5.5 lb. (2,500 Gm.) or less.

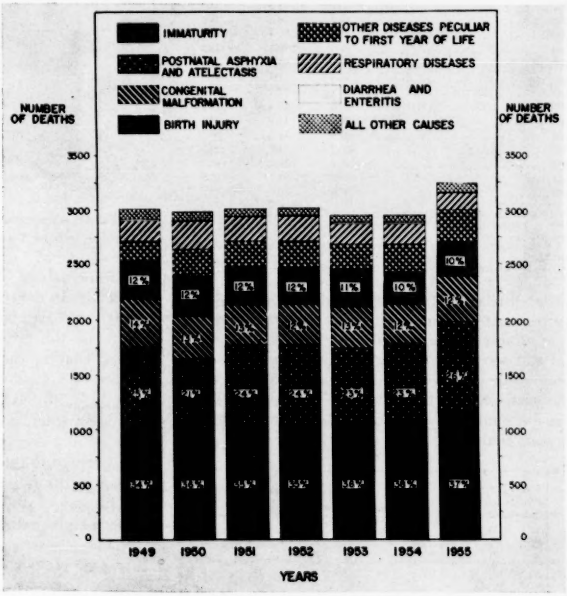

Fig. 3.—Neonatal deaths, by cause, in New York City, 1949-1955.

Since more than half of the early infant deaths occur in babies born prematurely, it is apparent that prematurity is a major cause of loss. Realizing its importance, the New York City Health Department 20 years ago spearheaded the development of a city-wide program for better care for the prematurely born infant. Since 1948, a complete program has been in operation[5]: a service picks the baby up in the home or hospital (when the hospital is not well equipped or staffed to take care of small premature infants) and transports him to a hospital which has a nursery that is specially equipped and staffed to care for such infants. He is transported

in an incubator in a specially designed ambulance, with every precaution to guard his safety and well-being, under the watchful eye of a specially trained public health nurse. He is followed up in his home after discharge. High standards of medical and nursery care are maintained in centers for premature infants where special care, nursing, and medical and social services are available for these small premature babies. When families cannot meet all the costs of care, the difference is made up so that there are no financial barriers to procuring the best care available.

TABLE 1.—*Perinatal Mortality Rates, Fetal Death Ratios, and Hebdomadal Death Rates, per 1,000 Deliveries, New York City, 1937-1955*

	Perinatal Mortality Rate*	Fetal Death Ratio†	Hebdomadal Death Rate‡
1937	45.3	26.3	20.2
1938	45.4	26.4	20.2
1939	43.2	23.9	20.3
1940	43.4	23.6	20.8
1941	41.4	23.3	19.1
1942	39.3	21.8	18.3
1943	38.2	20.9	18.1
1944	38.7	21.1	18.5
1945	37.9	20.2	18.5
1946	36.9	19.3	18.4
1947	34.5	17.9	17.3
1948	34.1	17.1	17.5
1949	32.6	16.4	16.7
1950	31.0	14.9	16.5
1951	30.5	14.8	16.1
1952	30.7	14.9	16.3
1953	29.7	13.9	16.2
1954	29.8	14.1	16.0
1955	30.8	13.5	17.7

* Deaths under 7 days + fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births + fetal deaths of 28 or more weeks' gestation.
† Fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births.
‡ Deaths under 7 days × 1,000 ÷ total live births.

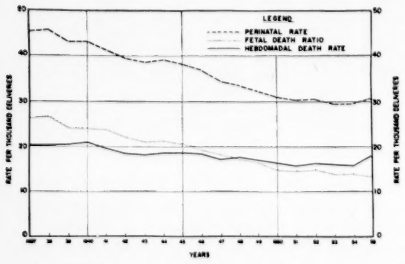

Fig. 4.—Perinatal mortality rate, fetal death ratio, and hebdomadal death rate in New York City, 1937-1955.

However, because existing centers are not able to meet all the demands, some babies are still deprived of this specialized care. It is figured conservatively that, in 1955, at least 550 more lives could have been saved if all babies had received the quality of care given in centers.

There is no question that the program for premature infants in New York City has paid dividends in saving lives, but what of the premature baby who survives the first month? What are his chances, compared to those of his full-term brother? The death rate in the postneonatal period of the prematurely born infant has shown no appreciable decline. In the smallest weight category, i. e., under 1,001 Gm. (2.25 lb.), the postneonatal mortality rate of the premature infant is 14 times greater than that of the full-term infant, in the 1,001 to 1,500-Gm. (2.25 to 3.25-lb.) group 10 times greater, in the 1,501-2,000-Gm. (3.25 to 4.25-lb.) group five times greater, and in the 2,001 to 2,500-Gm. (4.25 to 5.5-lb.) group, the most favorable weight group of premature infants, it is still 3 to 4 times greater than in the full-term baby.[6]

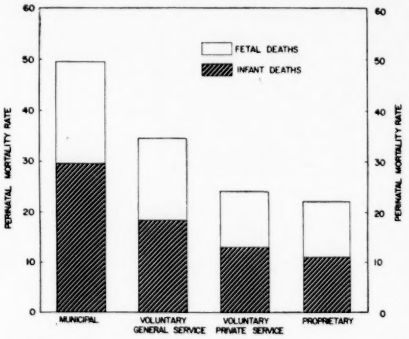

Fig. 5.—Perinatal mortality rate, by type of hospital and service, in New York City, 1955.

Intensive study of the factors contributing to these high postneonatal mortality rates is needed if improvement is to be effected. More careful and continued follow-up of the prematurely born infant after discharge from the hospital is essential. This aspect of the program for premature infants needs further strengthening, in addition to the expansion of premature centers to the needed capacity, so that no request for transfer of a premature baby need be denied.

TABLE 2.—*Live Births, by Ethnic Group, in New York City, 1950-1955*

	Total	Puerto Rican		Other White		Nonwhite	
		No.	%	No.	%	No.	%
1950	155,818	9,206	5.9	124,667	80.0	21,945	14.1
1951	162,755	10,479	6.4	129,096	79.3	23,180	14.3
1952	164,165	12,215	7.4	128,653	78.4	23,297	14.2
1953	161,499	14,431	8.9	123,093	76.2	23,975	14.9
1954	164,060	16,891	10.3	121,704	74.2	25,465	15.5
1955	165,150	18,365	11.1	119,692	72.5	27,093	16.4

The incidence of prematurity has also been found to be significantly higher in women who receive late and no prenatal care and in the unwed, both in our experience and in that of others. An increasing percentage of births in New York City is occurring

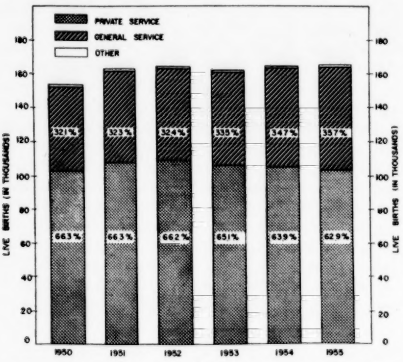

Fig. 6.—Live births, by type of service, in New York City, 1950-1955.

in these less-favored groups. We do not know precisely how socioeconomic factors work. The nutritional status of the mother is of some importance.

Of course, babies born to economically underprivileged Negro and Puerto Rican women tend to be smaller at birth and, though "full term," as judged by the length of gestation, may weigh 2,500 Gm. or less. The mortality rate of these "term infants" is higher than that of term infants weighing over 2,500 Gm.

What about the prevention of prematurity? Obviously, the basic difficulty is that so little advance has been made in knowledge of how to prevent premature labor and premature birth. Judging by the data on birth weights, no gains have been made in curbing premature births. In 1948, of the babies born alive in the city 8.8% weighed 2,500 Gm. or less. This percentage has been maintained in the years that followed and, in fact, rose to 9.2% in 1955, an increase which is statistically significant. Possible reasons for the failure to effect a diminution in premature births are indicated in certain associations, readily demonstrated in our figures. The drop in number of late fetal deaths, representing a possible carry-over into the liveborn premature group, has been mentioned. A higher incidence of prematurity, as judged by weight, occurs in the nonwhite or Puerto Rican groups as compared with the white, in the patients delivered on ward service as compared with private patients, and in the lower socioeconomic groups as compared with the upper socioeconomic groups.

These scattered epidemiologic observations and the few known clinical observations made on factors increasing the probability of premature labor do not yet furnish an adequate base of understanding of the mechanisms through which early labor is precipitated. Further elucidation is desperately needed. Common sense demands an enlarged and coordinated research attack on these fundamental problems.

Preventability of Perinatal Deaths

There is evidence that many perinatal deaths occurring today are preventable. This was clearly the conclusion of the study of a sample of the perinatal deaths made in 1950 and recently published by the New York Academy of Medicine.[7] This study, initiated at the suggestion of the Department of Health, was made with the cooperation of all hospitals and medical societies. On the basis of the careful analyses made, it was concluded that 35% of the perinatal deaths were preventable. The "pre-

TABLE 3.—*Perinatal Mortality Rates, Percentage of Live Births on General Service, Incidence of Prematurity, and Percentage of Live Births with Late or No Prenatal Care, New York City, 1955*

Geographic Area	Perinatal Mortality Rate*	% of Total Births: Delivered on General Service†	% of Total Births: Weighing Less Than 2,501 Gm.	% of Total Births: No or Late Prenatal Care‡
New York City, total	30.8	35.7	9.0	15.7
Manhattan, total	40.3	65.2	11.8	25.9
Central Harlem	51.1	92.4	16.3	39.5
East Harlem	34.9	78.4	10.7	29.4
Kips Bay–Yorkville	38.2	33.1	8.8	11.2
Lower East Side	32.7	55.2	10.1	21.7
Lower West Side	42.5	61.0	11.7	24.9
Riverside	42.3	65.7	12.4	29.4
Washington Heights	36.4	46.9	10.0	13.7
Bronx, total	30.3	39.0	9.0	13.6
Fordham–Riverdale	23.2	13.5	7.7	5.5
Morrisania	36.7	62.8	10.9	21.8
Mott Haven	39.0	60.8	10.1	21.8
Pelham Bay	24.1	19.4	7.4	6.9
Tremont	24.1	29.0	8.6	10.3
Westchester	28.4	20.3	7.5	7.7
Brooklyn, total	31.1	35.3	9.0	16.9
Bay Ridge	21.5	10.7	6.5	8.6
Bedford	41.1	66.2	13.1	26.5
Brownsville	35.8	35.0	9.0	18.6
Bushwick	30.3	33.2	8.3	16.9
Flatbush	25.3	8.6	7.6	8.6
Fort Greene	36.9	65.6	11.8	25.9
Gravesend	24.7	15.2	7.4	11.3
Red Hook–Gowanus	33.8	54.5	8.3	18.1
Sunset Park	27.7	24.3	7.0	11.0
Williamsburg–Greenpoint	34.3	48.0	9.4	24.7
Queens, total	24.9	15.6	7.5	8.7
Astoria–L. I. C.	25.4	20.7	6.8	9.1
Corona	24.9	16.5	7.5	8.6
Flushing	22.2	7.6	7.2	5.6
Jamaica East	28.7	29.0	8.7	14.3
Jamaica West	28.0	17.7	7.6	10.4
Maspeth–Forest Hills	21.0	5.6	7.4	5.0
Richmond	29.2	15.0	7.6	7.6

* Deaths under 7 days + fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births + fetal deaths of 28 or more weeks' gestation.
† Ward (nonprivate) service.
‡ Prenatal visit first made in 3rd trimester.

ventability" rates were consistently higher for deaths in ward-service cases than for deaths in private cases, as well as in mature babies compared with premature. They were also higher in nonteaching hospitals.

Hospital Care.—Conditions in some hospitals have long been found to be not conducive to the best care for mother and child.[8] In recent years there has been a marked improvement. This is clearly shown in the regular reports made by the hospital consultation teams composed of an obstetrician, a pediatrician, and a nurse under the aegis of the health department. These teams visit all hospitals with maternity services and confer with the hospital staff. A high standard for maternity and newborn infant care has been set by a section of the Sanitary Code, which has the force of law. In the past five years, physical conditions in the inpatient service have been much improved. Blood is now readily available for transfusions. Physical conditions and equipment are much improved.

An important part of this picture is the traditional close cooperation of the official health and hospital departments with medical schools, medical societies, voluntary hospitals, and several hospital groups. The Department of Health leans heavily on advisory committees, composed of leading obstetricians and pediatricians. The policies and recommendations made by them are widely distributed and have considerable influence. The local association of hospital superintendents has been helpful, particularly in improving inpatient services.

Despite all of these advances, serious problems still exist in hospitals, the most important of which is shortage of staff members. How can the continuing problem of shortage of qualified nursing personnel be met? How can ancillary staff be provided and trained to assume some duties formerly assigned to regular nurses? Why should "preventability" rates be higher in ward-service patients than in private, in nonteaching hospitals than in teaching?[7] Qualified residents and interns are in short

TABLE 4.—*Comparison of Districts with High and Low Perinatal Mortality Rates* and Selected Birth Characteristics, New York City, 1955*

	High Perinatal Mortality Rates					Low Perinatal Mortality Rates			
District	Perinatal Rate†	General Service,‡ %	Pre-maturity,§ %	Late or No Prenatal Care,‖ %	District	Perinatal Rate†	General Service,‡ %	Pre-maturity,§ %	Late or No Prenatal Care,‖ %
Total	30.8	35.7	9.0	15.7	Total	30.8	35.7	9.0	15.7
Central Harlem	51.1	92.4	16.3	39.5	Maspeth-Forest Hills	21.0	5.6	7.4	5.0
Lower West Side	42.5	61.0	11.7	24.9	Bay Ridge	21.5	10.7	6.5	8.6
Riverside	42.3	65.7	12.4	29.4	Flushing	22.2	7.6	7.2	5.6
Bedford	41.1	66.2	13.1	26.5	Fordham-Riverdale	23.2	13.5	7.7	5.5
Mott Haven	39.0	66.8	10.1	21.8	Pelham Bay	24.1	19.4	7.4	6.9

* Five districts with highest and five with lowest perinatal mortality rates.
† Deaths under 7 days + fetal deaths of 28 or more weeks' gestation × 1,000 ÷ total live births + fetal deaths of 28 or more weeks' gestation.
‡ Ward (nonprivate) service.
§ Weighing less than 2,501 Gm. at birth.
‖ Prenatal visit first made in 3rd trimester.

Sound consultation policies are now in effect in the majority of hospitals and have been considerably strengthened. The responsible directors of obstetric and of newborn infant services in hospitals are well qualified for their jobs and are, for the most part, in active charge of their respective services.

Just as the New York Academy of Medicine's study on maternal mortality in New York City in 1933[1] led to the formation of maternal mortality committees who reviewed all maternal deaths with the aim of calling attention to avoidable and needless mortality, the more recent study on perinatal mortality has stimulated the formation of perinatal mortality committees in the medical societies. Further, in many hospitals organized perinatal mortality conferences are now established in which the obstetric, pediatric, pathology, anesthesiology, and other related services participate. Much benefit is bound to accrue when the combined efforts and interest of the various groups are focused on a common aim of increasing knowledge concerning causes of death and preventing needless loss.

supply in a number of hospitals, especially in nonteaching hospitals. Medical schools and nurses' training schools must certainly be fostered and supported much more actively if standards of care are to be maintained—let alone advanced. New ways to use safely and effectively all kinds of more readily available ancillary personnel must be sought. Jobs must be analyzed so that precious professional time is not used for services given as effectively by those with less training. The patient should be added to the team. Providing safe anesthesia is still a problem in many hospitals.

Prenatal Care.—Prompt recognition, treatment, and prevention, wherever possible, of complications of pregnancy are of utmost importance for the welfare of the mother and the baby. The promotion of adequate and proper prenatal care is fundamental. It is disturbing to note that in New York City the incidence of late and no prenatal care has risen from 10.6% in 1951 to 15.7% in 1955 and that those districts where the highest incidence of prematurity

and perinatal deaths prevailed are the ones with the highest incidence of late or no prenatal care (table 4).

What accounts for this lack of prenatal care in a city where obstetric, medical, and public health facilities are plentiful? Are services so unattractive that people will not use them? Do the younger, underprivileged women not realize the protection that comes from early and continuing medical supervision? What needs to be done?

For one thing, as one visits hospitals one gets the impression that the outpatient service is the stepchild of the obstetric service and that there is too little continuity of care between inpatient and outpatient service. Prenatal clinics are, in the main, overcrowded and understaffed, have too few physicians in attendance, and often lack adequate obstetric supervision. It is not uncommon to find no attending physician present for guidance and consultation.

Need for More Knowledge and More Accurate Diagnosis of Cause of Death.—The Academy of Medicine's study [7] of perinatal deaths pointed up the need for clarification and recording of causes of death, as well as the need for more and better pathological study. In this study, in only 35% of the babies had an autopsy been performed. In many autopsies, only partial examination had been made. The clinical and pathological diagnoses frequently did not coincide. City-wide figures have corroborated these findings for many years.

The leading causes of neonatal deaths, as now cited, are (1) immaturity (37%), (2) postnatal asphyxia and atelectasis (26%), (3) congenital malformations (12%), and (4) birth injuries (10%). Other diseases peculiar to first year of life, a "catch-all" category, accounted for about 8% (fig. 3).

The importance of postnatal asphyxia and atelectasis has led the infant mortality committees of the Medical Society of Kings County and now of New York County to devote time and thought to the prevention of asphyxia and atelectasis, as well as the resuscitation of the affected newborn infant. A comprehensive and most useful report on resuscitation of the newborn infant has been prepared by the New York County Infant Mortality Committee.[9]

Congenital Malformation

What of the infant born with a congenital malformation, birth injury, or cerebral palsy? Accurate knowledge of the incidence of these conditions could be greatly improved. We know that the reporting on birth certificates is not adequate. Frequently, recognition of the condition is not made until after the birth record has been filed. Ways and means of obtaining a more accurate picture of the incidence of these conditions must be explored, along with ways to assure more adequate rehabilitation of the victim.

Congenital malformations account for 12% of the neonatal deaths and 26% of the postneonatal deaths. Little is known of the factors operating in the causation of these aberrations in development or function.

The maternal complications which can lead to loss of life of the fetus or baby are those which, short of killing, can also handicap the infant. As an example, hemorrhage due to premature separation of the placenta or toxemia in the mother may create a state of oxygen deficiency in the fetus, resulting in premature birth, in death, or in brain damage. The association of rubella in early pregnancy with the incidence of congenital anomalies in the offspring is well established. Other viral diseases may be implicated as well. Detailed correlative studies of the complications of pregnancy in relation to the outcome of pregnancy should add to our scant knowledge of this subject.

Our data indicate that congenital malformations occur with greater frequency in the prematurely born infant as compared with the full-term infant.[10] Cerebral palsy is likewise more often associated with premature birth.

Since more children survive, those orthopedic and musculoskeletal deformities that are seen more commonly in the premature infant are becoming relatively more prevalent. The emergencies of "saving the life" of the infant sometimes mean that the physician who is not well trained in orthopedic abnormalities overlooks some deformities. There is a real need for early diagnosis and early case finding of such abnormalities. Training general practitioners, obstetricians, pediatricians, and nurses to recognize obvious orthopedic abnormalities is indicated. A delay of a few months in treatment in such conditions as congenital dislocation of hip may cause a permanent deformity which could have been prevented by early diagnosis and treatment.

What Lies Ahead

This, then, is the general picture of perinatal mortality in New York City. What lies ahead?

Research.—Obviously, with so large a proportion of the deaths in this age-period attributable to causes for which means of prevention are as yet unknown, an augmented and carefully balanced research program has high priority. The problems are social in nature, as well as medical. Research projects must utilize the skills of persons trained in different fields—obstetricians, pediatricians, sociologists, statisticians, geneticists, pathologists, anthropologists, nutritionists, physiologists, biochemists, and anatomists. Carefully planned, on-going

longitudinal studies are of primary importance, because so much of our current knowledge is based on retrospective studies. For many years, the National Institutes of Health supported little research in this important field. It is to be hoped that the more recently established studies related to a better understanding of human reproduction will become an important part of the research programs financed by federal tax funds.

Aside from the basic research that needs to be done on the methods of preventing loss of life associated with pregnancy, there are practical "operational" research projects of one sort or another that will be useful. These should tackle such problems as finding ways to use existing personnel more effectively, ways to appeal to the woman who does not seek prenatal care, and ways to develop meaningful and acceptable preconceptual services.

Immediate Steps.—While we are waiting for better answers to these ancient problems, what specifically can professional and lay groups interested in reducing perinatal mortality do in New York City as of now? We have four suggestions to make.

First, the 15% of women now receiving late or no prenatal care under medical supervision should be seen early enough in pregnancy that they can benefit from that care. This will involve better methods of case-finding and better follow-up, and certainly the prenatal clinic must be brought "out of the basement," literally and figuratively. A new interest on the part of general practitioners, hospital superintendents, and obstetricians in prenatal care will do much to bring all pregnant women under prenatal care early in pregnancy.

Second, we need to strive for better teamwork in the maternity services—better teamwork among general practitioners, obstetricians, pediatricians, nurses, ancillary workers of all kinds, and medical specialists of all kinds. The well-organized perinatal mortality conference in every hospital is a step in the right direction. Bringing the physiologist, pathologist, geneticist, sociologist, and nutritionist in at appropriate times may help. The orthopedist and the cardiologist, for instance, need to be brought in earlier to help with the handicapped baby. And, perhaps most important of all, letting the prospective parents themselves in on "the team" should bring rich rewards.

Third, New York City needs to complete the job of providing facilities for the prematurely born infant. This means putting into active operation all the beds located in currently approved centers for premature infants and developing the additional small numbers of centers that are needed.

Finally, we must pay special attention to the emergency problems created by the migration of so many underprivileged people into the city. This is not really a new problem. Every time there has been an immigration of people of lower socioeconomic groups, special efforts had to be made in their behalf. Infant mortality had always been high in this group—high until they got the kind of housing, jobs, medical care, and food they needed and until their language barriers were overcome. The help and interest of enlightened people in the community have always solved these problems. The basic question is this: Will we in the greatest and perhaps richest city in the world give economically underprivileged babies the same chance for life and health that other babies have?

125 Worth St. (13) (Dr. Baumgartner).

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DEATHS AROUND BIRTH—THE NATIONAL SCORE

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A comparison of the mortality figures for 1915 with those for 1955 shows that during this interval both maternal and infant mortality rates have been strikingly reduced. Maternal deaths have been reduced from 60 to 5 per 10,000 live births, and the infant mortality rate has dropped from 100 to 26 per 1,000. Further reduction is possible and necessary, for the frequency of perinatal and maternal losses was fourth among main causes of death at all ages in 1955 in the United States. The causes of perinatal mortality need to be identified because they must also be the causes of congenital handicaps in millions of infants who do not die. Differences in mortality between urban and rural patients and between different socioeconomic strata prove the importance of environmental factors. Preventing prematurity and improving the care of premature infants are among the immediate problems. For continued progress in the reduction of perinatal mortality it will be necessary to make sure that children who are to be the parents of the future grow up as members of healthy families in the best possible environment.

Death is associated with birth and being born in the United States more often than it is with any disease except heart disease, cancer, and cerebral hemorrhage. These deaths are among the most tragic, since they cut off life at its beginning or take a mother away from her family. In 1955, deaths in childbearing and being born numbered an estimated 165,376, of which 1,901 were maternal deaths, about 86,124 were deaths of infants before or during birth (if we take account of underreporting of such deaths), and 77,351 were deaths of liveborn infants in the neonatal period.[1]

Mortality, we know, is not the whole toll from sickness and misadventure in childbearing and being born. The aftermath for the mother may be chronic illness or repeated reproductive failure; for the infant, it may be irreparable damage, such as we see in children who suffer from cerebral palsy, epilepsy, mental retardation, and congenital malformations. In the United States today, mortality of the infant in the perinatal period, that is, in the period before, during, and soon after birth, is of vital concern to all who seek to conserve new life or who see in these fatalities a threat to continuing health in mothers and children.

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167

Because there is much concern today with problems of maternal morbidity which result in premature delivery and with the causes of fetal and neonatal deaths, particularly those associated with congenital malformation, primary attention is given in this report to the whole perinatal period continuing to the end of the first month of postnatal life. The term perinatal mortality, as used here, embraces deaths of infants before or during birth (fetal death) in pregnancies of 20 weeks' duration or more and deaths of liveborn infants in the neonatal period (under 28 days), regardless of duration of the mother's pregnancy. This perinatal mortality rate is the number of such fetal and neonatal deaths per 1,000 births of live or stillborn infants. This rate is useful, since it helps us to view as a whole infant losses among mothers whose pregnancies are relatively advanced. Within this span, different intervals may be focused on separately, depending on the problem under study.

Perhaps at this point we should look back to see how far we have come in safeguarding mothers and babies during the maternity cycle and the first year of the infant's life. One of the reasons for the establishment of the Children's Bureau in 1912 was a nationwide concern about the deaths of infants and women during pregnancy and childbirth. At that time, the national score on infant and maternal mortality was not known. It was for this reason that one of the first activities of the young Children's Bureau was to work with the Bureau of the Census and the General Federation of Women's Clubs in establishing the birth registration area.

The first score was obtained in 1915. Although based on data from only a few states, it showed clearly that far too many mothers and babies were dying. For every 1,000 live births, six mothers died, and 100 infants, 1 out of 10, did not live to see their first birthday.

As we compare today's scores with those of 1915, we can feel considerable satisfaction in the accomplishments of the last four decades. Instead of six maternal deaths in 1,000 live births, now there are nearer five in 10,000. The infant mortality rate has dropped from 100 to 26 per 1,000. Seen in retrospect, the national score in 1955 looks extremely good.

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Read at the 57th Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

Improved sanitation and standards of living, better nutrition, important discoveries in medicine, more and better hospital care and other health services—all these have contributed to this great

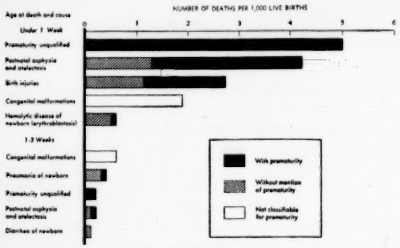

Fig. 1.—Early infant deaths by age and cause, United States, 1955 (data from National Office of Vital Statistics).

saving of life. But, unfortunately, these benefits have not extended equally to all parts of the United States or to all groups of the population.

In many localities in the United States, progress in reducing infant and maternal mortality lags behind that for the country as a whole. For example, in isolated counties with no cities of 50,000 or more, the average annual infant mortality rate in the period 1951-1954 was 17% higher than that in counties with such cities.

Most of the reduction in the national infant mortality score has been due to a decrease in deaths after the first month of life. These have dropped from about 56 per 1,000 live births in 1915 to just over 7 in 1955. This saving of life has come about largely through the prevention and control of infectious and gastrointestinal disease.

But the death rate in the first month of life has dropped much more slowly. As we look at the principal causes of death in the neonatal period, we find that infectious and gastrointestinal disturbances are not important in the picture. The five main causes to which deaths in the first and later weeks of the neonatal period were attributed are illustrated in figure 1. Mortality rates for these and other causes in the neonatal period are shown in table 1. The causes are prematurity, postnatal asphyxia and atelectasis, birth injuries, congenital malformations, and hemolytic disease of the newborn, which results chiefly from Rh incompatibility. The conditions responsible for these early infant deaths nearly all have their origin before or during birth and are, for the most part, associated with morbidity in the mother.

TABLE 1.—*Neonatal Mortality Rate per 1,000 Live Births by Age and Main Causes of Death, United States, 1955**

Cause of Death†	Neonatal Death Rate‡ Total	Under 1 Wk.	1-3 Wk.
All causes	19.1	17.0	2.1
Certain diseases of early infancy 760-76	15.4	14.2	1.2
With immaturity (.5)	11.4	10.8	0.6
Without mention of immaturity (.0)	4.0	3.4	0.6
Immaturity unqualified 776	5.2	5.0	0.2
Postnatal asphyxia and atelectasis 762	4.3	4.1	0.2
Birth injuries 760-1	2.9	2.8	0.1
Pneumonia of newborn 763	0.8	0.4	0.4
Hemolytic disease of newborn (erythroblastosis) 770	0.6	0.6	0.0
Neonatal disorders arising from maternal toxemia 769	0.1	0.1	0.0
Hemorrhagic disease of newborn 771	0.2	0.2	0.0
Diarrhea of newborn 764	0.1	0.0	0.1
Other and ill-defined diseases of early infancy, including nutritional maladjustment 765-8, 772-4	1.2	1.0	0.2
Congenital malformations 750-9	2.5	1.9	0.6
Influenza and pneumonia (except pneumonia of newborn) 480-93	0.0	0.0	0.0
All other diseases of respiratory system 470-5, 500-27	0.3	0.3	0.0
All infective and parasitic diseases 001-138	0.1	0.0	0.1
Gastritis, duodenitis, enteritis, and colitis (except diarrhea of newborn) 543, 571-2	0.0	0.0	0.0
Accidental mechanical suffocation in bed or cradle E924	0.0	0.0	0.0
All other accidental causes E800-923, E925-62	0.1	0.1	0.0
Other specified conditions Residual	0.4	0.3	0.1
Symptoms and ill-defined conditions 780-95	0.3	0.2	0.1

* Exclusive of fetal deaths.
† Numbers refer to categories in 6th Revision of International List.
‡ Under 28 days.

But the death rate in the first month of life has dropped much more slowly. As we look at the principal causes of death in the neonatal period, we find that infectious and gastrointestinal disturbances are not important in the picture. The five main causes to which deaths in the first and later weeks of the neonatal period were attributed are illustrated in figure 1. Mortality rates for these and other causes in the neonatal period are shown in table 1. The causes are prematurity, postnatal asphyxia and atelectasis, birth injuries, congenital malformations, and hemolytic disease of the newborn, which results chiefly from Rh incompatibility. The conditions responsible for these early infant deaths nearly all have their origin before or during birth and are, for the most part, associated with morbidity in the mother.

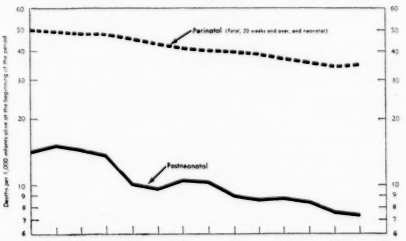

Fig. 2.—Reduction of perinatal death rate compared with that of postneonatal death rate, United States, 1942-1955 (data from National Office of Vital Statistics).

At least three out of five neonatal deaths are in infants whose mothers' pregnancies do not run to normal term. Although premature delivery is not usually thought of as evidence of maternal morbibity, surely some abnormality causes a mother to give birth before term. Premature delivery increases the risk of death in the newborn infant 20 times.[2]

The trend lines in figure 2 show the perinatal death rate and death rate for infants surviving the first month of life from 1942 to 1955. While the postneonatal mortality rate was cut in half, the perinatal mortality rate was reduced less than one-third. The perinatal death rate is now five times that of infants after the first month of life. In table 2 are given mortality rates for each of several intervals within the perinatal period and for the postneonatal period during these years. Each rate is based on the number of infants alive at the beginning of the particular interval.

An indication of the national importance of present perinatal and maternal losses can be seen in figure 3, where the frequency of such deaths is fourth among main causes at all ages in 1955 in the United States.

More and more evidence is accumulating that the same conditions that bring death to infants before, during, and soon after birth also may lead to chronic illness and handicap in many infants who survive. We do not know accurately how many children may suffer such results. But, from the limited information, a rough estimation is that probably 315,000 children have cerebral palsy,[a] 310,000 epilepsy, and 1,500,000 mental retardation. Something like 285,000 infants with congenital malformations are born each year (these estimations were made by the Children's Bureau to take into account underreporting).

More research is needed to discover how such chronic illness and handicap are related to the 350,000 premature deliveries that occur to mothers of liveborn infants each year, to other complications of pregnancy, labor, and delivery, or to the diseases and defects that each year take an estimated 163,475 infant lives in the perinatal period.

The greatest hazards to the baby occur just before birth and during his first three days of life (fig. 4 and table 2). Since most of the babies who die soon after birth are born prematurely, our best chance to reduce deaths in these first few days lies in finding effective ways of insuring that the mother can carry her baby to term.

While fatal risks in the first 3 days of life have been cut very little since 1942 (17%), the neonatal death rate for infants surviving these days has been reduced 46% since 1942. No doubt this reflects, at least in part, improvement in the care of newborn infants, especially in the care of premature infants.

In recent years, more than half of the states and territories made some special effort in behalf of premature infants through their maternal and child health programs. Twenty-one were either supporting special services for premature infants or otherwise contributing to development of good hospital care for these infants. While much has been and is being done to improve care of such immature infants, much more remains to be done.

TABLE 2.—*Perinatal Mortality Rates per 1,000 Infants to End of First Month of Postnatal Life and Infant Mortality Rate by Age, United States, 1942-1955**

	Perinatal Period†					
			Neonatal Death Rate (Under 28 Days)‖			
	Total‡	Fetal Death Rate§	Total	Under 3 Days	3-27 Days	Post-Neonatal Period (1-11 Mo.)¶
1955	35.6	16.8	19.1	14.7	4.4	7.4
1954	35.9	17.2	19.1	14.4	4.7	7.6
1953	36.7	17.5	19.6	14.6	5.0	8.4
1952	37.4	18.0	19.8	14.8	5.1	8.8
1951	38.1	18.5	20.0	14.9	5.2	8.6
1950	39.0	18.8	20.5	15.3	5.3	8.9
1949	40.5	19.4	21.4	15.7	5.9	10.1
1948	41.9	20.2	22.2	16.1	6.2	10.1
1947	42.9	20.6	22.8	16.3	6.6	9.6
1946	45.8	22.3	24.0	17.1	7.1	10.0
1945	47.2	23.4	24.3	16.6	7.8	14.3
1944	48.0	23.9	24.7	16.8	8.0	15.5
1943	48.1	23.9	24.7	16.9	8.0	16.0
1942	50.0	25.0	25.7	17.7	8.1	15.1

* Deaths of live-born infants in specified age group and deaths before or during birth (fetal deaths) of infants born to mothers pregnant 20 or more weeks, or duration unreported. In 1955, all states except Rhode Island required reporting of fetal deaths in pregnancies of 20 or more weeks' duration; Rhode Island required reporting at six completed months or more of pregnancy. For requirements by state in other years, see "Vital Statistics of United States," published annually by National Office of Vital Statistics.

† For liveborn infant, beginning of perinatal period is coincident with or prior to onset of labor (or other termination of pregnancy).

‡ Number of fetal and neonatal deaths per 1,000 births (live and still).

§ Number of deaths before or during birth per 1,000 births (live and still).

‖ Prior to 1949, neonatal period was under 30 days. Rate under 3 days of postnatal age is per 1,000 live births; for age groups 3-27 days, rate is per 1,000 infants surviving three days of postnatal life.

¶ Number of deaths of infants 1-11 months of age per 1,000 surviving first month of postnatal life.

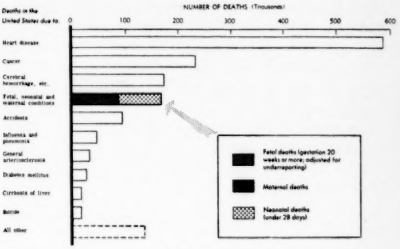

Fig. 3.—Comparison of fetal, neonatal, and maternal conditions causing death with other causes, United States, 1955 (data from National Office of Vital Statistics).

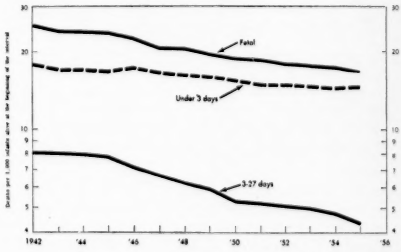

Fig. 4.—Reduction in deaths soon after birth compared with that for rest of perinatal period, United States, 1942-1955 (data from National Office of Vital Statistics).

Since 1942, the fetal death rate in the latter half of pregnancy has been reduced by nearly a third, from 25.0 to 16.8 per 1,000 births, live and still (see table 2). Presumably, this is the result of better prenatal and obstetric care of mothers. Mothers have a better chance today of giving birth to a living child than they had a decade ago. Some infants

who formerly would have died in utero or during labor are born alive. Many of them survive, though some are too feeble for independent existence and die within a few days.

The volume of perinatal loss recorded in 1955 in the United States is shown in table 3 in relation to detailed age at neonatal death and duration of pregnancy in which fetal death occurred. Over half the neonatal deaths (52%) were on the first day of life; 89% occurred in the first week, 6% in the second, 3% in the third, and the remaining 2% in the last week of the neonatal period. Of the 69,153 fetal deaths recorded in 1955 in pregnancies of 20 or more weeks, 32% were in those reported as enduring 40 or more weeks.

How can we attack the problem of carrying infants safely through the perinatal period? Research is one answer. Not only do we need research to discover how various handicapping conditions of

TABLE 3.—*Perinatal Mortality to End of First Month of Postnatal Life by Age at Neonatal Death, Duration of Pregnancies Resulting in Fetal Death, and Color, United States, 1955**

Age at Neonatal Death, Days, and Duration of Pregnancy, Wk.	Deaths, No.		
	Total	White	Nonwhite
Total perinatal period	146,504	113,751	32,753
Neonatal death (under 28 days)	77,351	61,340	16,011
<1 wk.	68,654	55,140	13,514
<1 day	40,480	32,316	8,164
1 day	11,692	9,643	2,049
2 days	7,449	6,165	1,284
3 days	3,783	3,043	740
4 days	2,232	1,722	510
5 days	1,739	1,285	454
6 days	1,279	966	313
1 wk.	4,374	3,196	1,178
2 wk.	2,475	1,766	709
3 wk.	1,848	1,238	610
Fetal death	69,153	52,411	16,742
20-27 wk.	16,200	11,781	4,419
28-31 wk.	8,557	6,299	2,258
32-35 wk.	9,035	7,118	1,917
36-39 wk.	13,187	10,485	2,702
40+	22,174	16,728	5,446

* Deaths of live-born infants in specified age groups and deaths before or during birth (fetal deaths) of infants born to mothers pregnant 20 or more weeks, or duration unreported.

childhood are related to maternal and perinatal illness and defect but we also need knowledge of the whole chain of events underlying these conditions.

Understanding the reproductive process calls for many different approaches. One approach, animal research, is producing important clues as to possible causes of congenital defects. We need many more such studies, together with studies showing the application of these findings to human beings.

Another approach lies in clinical and pathological studies of untoward conditions during pregnancy and follow-up studies of surviving infants. For example, what are the causal factors in bleeding in early pregnancy, and how does this affect the fetus? Or, what are the significant events associated with premature labor? True, we know some of them, but, for the majority, we can only guess. In a study at Johns Hopkins University of premature deliveries, no explanation could be found in 60% of the cases.[4]

The clinical and public health approaches to these problems can be combined in forward-looking studies of successive pregnancies from the beginning of each pregnancy through delivery with long-term and regular follow-up of the mother and her children. This is one way physicians can learn more about the immediate and long-run bearing of specific events in early pregnancy on the health of the mother and the development of her child. Studies of this sort are now being initiated in a number of clinics.

Obviously, research on reproduction calls for the knowledge and skills of many scientific disciplines: obsterics, pediatrics, pathology, chemistry, physiology, embryology, genetics, biostatistics, public health administration, and others.

Many investigators believe that, although each of these specialties has its own approach to these studies, all specialists can work more fruitfully if their efforts are coordinated. This does not necessarily mean coordination through formal plans and agreements, but, the kind of coordination that occurs from exchange of ideas and from joint thinking about the problem when different approaches intersect or overlap.

Of some things we are certain. We know that good care for infants born prematurely saves many who would not survive otherwise. Services to provide such care should be available wherever infants are born.

We recognize the need for more extensive and more effective maternal and child health services, especially in rural areas and for the less fortunate socioeconomic groups. But just what is meant by more effective services? For one thing, a program that accepts prenatal care as one of its major functions is necessary. An analysis of the way public health nurses use their time shows that 40% of it is devoted to maternal and child health, but, of this, only 10%–4% of the total time—is given to prenatal care.

More attention needs to be given to finding those expectant mothers who are less likely to seek care for themselves and who more often need intensive service. And we can give thought and study to how the nursing visit can be most meaningful.

Continuity in care throughout pregnancy and labor and the postpartum and interpregnancy periods is essential to the best maternity care. Commonly, continuity in medical care for the pregnant woman is provided by physicians in their private practice. The support and supervision thus given may be even greater if the plan of care provides also for visits to the family by a public health nurse. Often, however, when a mother seeks maternity care in a hospital or other clinic this continuity of medical care does not exist. She may be seen by

more than one physician during a single pregnancy and be delivered by still another. Between pregnancies she may not be seen at all by either physician or nurse. Much attention needs to be given to this aspect of maternity care if premature delivery and perinatal mortality are to be reduced.

Studies of obstetric case histories usually reveal a certain proportion of women who have had repeated unsuccessful pregnancies. For a physician to dismiss such a woman after her postpartum examination may mean he is dismissing her at a time that she most needs study and treatment. By the time her next pregnancy is confirmed, it may be too late to do anything about helping her carry her baby to term.

In cases where a woman has had one or more unsuccessful pregnancies, careful diagnostic study of both husband and wife are indicated, with treatment as necessary, before another pregnancy occurs. The treatment may be psychological, nutritional, or physical, with endocrine therapy when needed. Such study and treatment are best carried out by a team—physicians, nurses, social workers, nutritionists, and psychologists—each member contributing an important share.

An aspect of prenatal care too often neglected is the provision of hospital care when complications of pregnancy occur. Where good hospital care is available, a woman with toxemia or threatened abortion can often be carried through until the infant becomes mature enough to have a good chance for survival. Or, if toxemia in later pregnancy is too severe, the premature induction of labor may prevent a fetal death, possibly even a maternal death.

A few state health departments now make funds available for hospitalization of women with complications of pregnancy. These funds can be used more effectively in a program which has a carefully developed referral system and nursing follow-up.

For another thing, we need services directed especially to the socioeconomic groups that are most vulnerable. In Denver, a study of the women admitted to the hospital because of complications of pregnancy showed that a large proportion came from an area of low socioeconomic development in which the general health level was low. At the University of Aberdeen, Scotland, where nearly all of the women received the same maternity care, premature birth and perinatal death were found more often in infants of mothers from the lower socioeconomic groups than they were in those of upper social groups.[5]

In the United States, we have evidence that perinatal mortality is affected by the socioeconomic status of the mother. Perinatal losses are higher for the nonwhite population than for the white; the fetal death rate is 85% higher among nonwhite mothers than among white, and the perinatal rate more than 67% higher than for white (table 4). While some of these differences reflect the younger age and larger families of nonwhite mothers, undoubtedly they also represent differences in economic status and deficiencies in early and present environment. Similarly, in the careful study on incidence of congenital malformations reported from Babies Hospital and Sloan Hospital for Women in New York City, a significantly higher incidence was found among nonwhite as compared with white infants.[6]

Summary

Today, the greatest loss of infant life occurs around the time of birth. Much of this fatality could be prevented if present knowledge were more widely and intensively applied. Medical, nursing, and hospital services should be more readily available outside of cities. Too few good hospital services exist for premature infants. Maternity services should seek out and give special attention to the woman who has already had an unsuccessful pregnancy when, or even before, she becomes pregnant again. Early environment may affect a woman's ability to bear children successfully. Consequently, we must concern ourselves with the nutrition and health of all of the family if little girls growing up today are to be bearing healthy babies tomorrow.

TABLE 4.—*Perinatal Mortality Rate to End of First Month of Postnatal Life by Color, United States, 1955*

	White	Nonwhite	Ratio	Total
Perinatal rate per 1,000 births (live and still)	32.4	54.1	100:167	35.6
Fetal rate per 1,000 births (live and still)	14.9	27.6	100:185	16.8
Neonatal rate (under 28 days) per 1,000 births (live)	17.7	27.2	100:154	19.1

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Marian M. Crane, M.D., and Eleanor P. Hunt, Ph.D., of the Division of Research of the Children's Bureau, participated in the development of this report.

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CHALLENGE OF FETAL LOSS, PREMATURITY, AND INFANT MORTALITY—A WORLD VIEW

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Comparison of data from various countries shows that large differences exist with respect to the loss of human life from premature births, deaths during the neonatal period, and deaths in the age period from one month to 4 years. Attention is called particularly to the very high death rates in the age group of 1 to 4 years in economically less developed areas. The differences are seen to be largely correctable. This is proved not only by contemporary comparisons of country with country but also by comparison of past with present mortality rates in countries where adequate records have been kept. Three phases of action are suggested to reduce this loss of human life: A first point of attack is to establish and strengthen basic public health services, including maternal and child health services, in economically less developed areas. A second is a series of specific measures to reduce prenatal and neonatal mortality, for instance, by improved prenatal care and by improved treatment of premature infants. A third is an intensive program of research aimed at the identification and correction of all factors that may handicap a child in either its intrauterine or its postnatal growth. The first measure is essential for the reduction of excessive mortality in the age period 1 month to 4 years. The second and third measures are increasingly important in the reduction of perinatal mortality.

In dealing with fetal loss, prematurity, and infant mortality on a world basis, it is advisable to consider this subject within the framework of the problem of mortality in childhood throughout the world. Although risk of death diminishes as children advance in age, in many areas of the world death rates are not only high in infancy but continue to be so in early childhood, becoming much lower only at school age. There is great variation between economically developed and less developed countries. Grouping the latter, which represent three-fifths of the population of the world, approximately 50% of all deaths are of children under 5 years of age, while in the technically advanced countries, including one-fifth of the world population, only 10% of the deaths are in this age group.[1]

Variation in Death Rates

The situation regarding mortality in infancy and early childhood is presented in figure 1, which shows death rates for children under 1 year and for those 1-4 years of age for 25 selected countries of the world (derived from the Demographic Year Book of the United Nations for years up to 1954, the Annual Epidemiological and Vital Statistics of the World Health Organization [WHO] for years up to 1952, and annual and special reports of these agencies and countries). There is an association between high rates and low economic development, and attention is called particularly to the very high death rates in the age group of 1 to 4 years in economically less developed areas.

In order to focus attention on the problems of the present discussion, variations in fetal, neonatal, and postneonatal (1-11 months) death rates per 1,000 live births are shown for the same countries (fig. 2). The data are highly unequal in quality, particularly with regard to fetal loss and neonatal mortality. Here, differences are the result of gross incompleteness of registration in some countries in addition to the variation due to differences in definition of fetal deaths and live births. In spite of the inaccuracies, the variation in neonatal mortality in these 25 countries is substantially less than the variation in postneonatal mortality. Also, if accurate data could be obtained for fetal deaths, it is probable that differences would be similar to those noted in the neonatal period. The lesser variation seen in the neonatal period and assumed for the fetal period can be related to the fact that the external influences have less effect on the fetus and the newborn infant than on the child in the subsequent months of his life. Therefore, the greater variation seen in the postneonatal period is a reflection of the influence of the environment, and the marked decline in postneonatal mortality in the technically developed countries is the result of improved health conditions and, in general, of the improvement of socioeconomic conditions. Following the decline in infant mortality, due to the reduction of the causes of death in the postneonatal period, the problem of wastage of life becomes centered on birth in the

From the Pan American Sanitary Bureau, Regional Office of the World Health Organization.
Read before the Annual Meeting of the Association for the Aid of Crippled Children, New York, April 30, 1956.

prenatal, natal, and neonatal period. Thus, in Chile, where the infant death rate is high, 51% of the wastage of life up to one year in 1952 occurred in the prenatal and neonatal period, while in Sweden 86% of the loss occurred in the same period.

To demonstrate changes over a period of time, fetal and infant death rates (fig. 3) are shown for three countries [2] over a period of nearly 40 years.

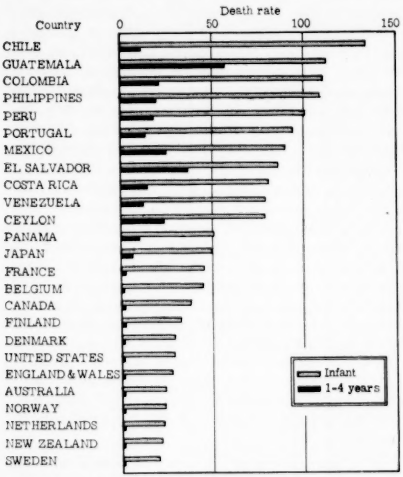

Fig. 1.—Infant deaths per 1,000 live births and deaths of children 1-4 years of age per 1,000 population for 25 selected countries, 1952.

The lower limits for registration of fetal deaths were as follows: in Sweden, fetuses no less than 35 cm. long; in the Netherlands, fetuses of at least 26 weeks' gestation before 1950, and, in 1950, 28 weeks' gestation and 35 cm. long; and, in the United States, 20 weeks' gestation. Rapid decline is evident in infant mortality and a slower decline in neonatal mortality and in fetal loss. Within the neonatal period the decline occurred mainly in the period of 1 through 3 weeks, whereas the death rate under one week has remained almost constant. The stability of mortality in the first week of life is further illustrated by the fact that, in the Netherlands in the last five months of World War II, the tremendous increase in infant mortality was only partially reflected in neonatal mortality and not in mortality of infants under one week of age.

The mortality in the prenatal period and soon after birth is commonly called perinatal mortality. The limits used for this mortality period vary at present and result in difficulties in analysis of data. We recognize that the causes determining this mortality are often interrelated and have their roots in circumstances early in the life of the mother, while they may also determine for the child increased hazards or handicaps for growth and development. Yet their direct impact on mortality is essentially measurable only within a limited period. In considering this problem, the WHO Study Group on Perinatal Mortality [3] expressed the desirability for uniformity and made the following statement: "It would seem that the age of practical viability, usually set at 28 weeks of gestation, could reasonably establish the lower limit, and since the majority of deaths in the neonatal period . . . occurs in the first week (a time when perinatal and natal influences still dominate and before the exogenous forces of such wide variance make their influence felt) the upper limit could be set at the end of the first week of life." These limits would provide data for a minimum period which, on a world basis, would have greater comparability than data for a more extended period. There is justification for this in the fact that late neonatal mortality (1-3 weeks) from exogenous causes is much greater when countries have high infant mortality. While in 1915 32%

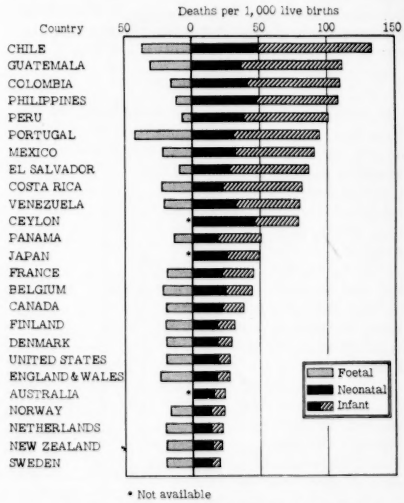

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Fig. 2.—Fetal, neonatal, and infant deaths per 1,000 live births for 25 selected countries, 1952.

of the neonatal mortality in the United States and 44% in Sweden occurred after the first week of life, in 1952 the corresponding percentages were 13 for both countries.

Variation in perinatal mortality and its relative importance in wastage of life is illustrated for six countries at different stages of development (table 1). These countries are selected for comparability

of data, are those with registered fetal deaths having the lower limit of 28 weeks' gestation, termed "late fetal deaths," [4] and are those in which deaths under 7 days were recorded. Their perinatal mortality rates vary from 27.1 to 63.4 per 1,000 total births. (The denominator recommended for the calculation of perinatal mortality is total births, which is the number of fetal deaths plus the number of live births.) Furthermore, mortality during this period was over 70% of the total loss in the fetal and infant periods in three countries (United Kingdom, the Netherlands, and Norway) and less than 40% in two countries (Chile and Costa Rica).

TABLE 1.—*Fetal, Perinatal, and Infant Death Rates for Six Countries, 1952*

Country	Fetal Deaths per 1,000 Total Births	Deaths Under 1 Wk. per 1,000 Total Births	Infant Deaths per 1,000 Live Births	Perinatal Deaths* per 1,000 Total Births	Perinatal Deaths* % of Total Fetal and Infant Deaths
Chile	35.9	27.5	133.6	63.4	38.5
Costa Rica	21.3	13.1	80.2	34.4	34.4
Canada	17.7	17.5	38.0	35.2	64.0
United Kingdom†	23.1	15.1	28.4	38.2	75.1
Norway	15.3	11.8	23.7	27.1	70.1
Netherlands	18.2	12.6	22.4	30.8	76.4

* Late fetal deaths and deaths under 1 week.
† Excluding Northern Ireland.

Causes of Mortality

In order to understand the underlying mechanisms that govern the reduction or lack of reduction of mortality, figures 4, 5, and 6 show data regarding the major groups of causes of deaths in infancy and childhood for selected countries. Death rates in the age group of 1 to 4 years are very low for the United States, Sweden, and Australia in comparison with the three others, indicating the extreme reducibility of death rates in this period of life.

In the first year of life (fig. 5), mortality [1] is also greatly reduced in the same three countries but not to the same extent. The reduction in mortality in these two age groups is determined essentially by three major groups of causes, namely, digestive diseases, respiratory diseases, and infective and parasitic diseases. However, in infancy there is residual mortality, due to a group of causes—congenital malformations and diseases of early infancy—which has not been greatly reduced even in the three countries with low infant mortality. The data for neonatal mortality (fig. 6) have to be interpreted with great caution because in countries with limited medical facilities the quality of certification of causes of death is poor. For the three countries with high rates, the data for Venezuela are probably the most reliable, since the rates were estimated on the basis of the distribution of 47% of the deaths medically certified. The great divergencies in the two others reflect essentially the poor quality of certification. Nearly all of the deaths in this neonatal period are due to the group comprising congenital malformations and diseases of early infancy, particularly in the United States, England and Wales, and Australia. This group may be considered in four subdivisions, namely, congenital malformations, birth injuries, other diseases peculiar to early infancy and immaturity unqualified, and infections of the newborn infant. The low rates for Ceylon for infections of the newborn infant, birth injury, and congenital malformations probably indicate that these causes were not stated on certificates, thus enlarging the proportion assigned to the less specific group "other diseases of early infancy." Some of these causes of death, such as pneumonia and diarrhea of the newborn infant, are more readily preventable, but the majority of deaths in the countries with low rates are difficult to prevent because of the underlying influence of immaturity.

Data on causes of fetal deaths are often unsatisfactory. Certain causes, such as birth injury and congenital malformations, influence both fetal and neonatal mortality, pointing to the interrelationship of causation.

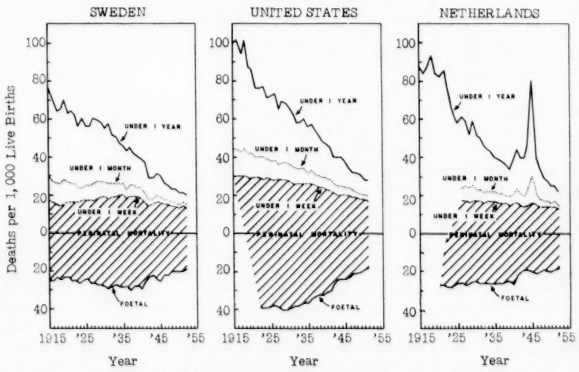

Fig. 3.—Fetal deaths and deaths of infants under one week, one month, and one year of age for Sweden, United States, and Netherlands, 1915-1952.

Analysis of data for Birmingham, England (table 2) shows, for instance, how certain causes play a role throughout the fetal and neonatal periods, while other specifically influence one period. Thus, toxemia and separation of the placenta influence mortality in both periods primarily in premature

infants. On the other hand, intranatal causes—essentially, birth trauma—influence both the fetal and neonatal mortality principally in the mature infant.

Mortality and Birth Weight

The condition of the infant at the time of birth is greatly influenced by his maturity, and prematurity plays an important role in both fetal and neonatal deaths. Although length of gestation is the most accurate measure, the generally accepted and most practical measure of maturity is birth weight. It is, therefore, important to consider its distribution and variation. For a number of years, the differences in average birth weights were attributed primarily to innate host factors, such as race and sex of the child, and the variations by birth order, age of the mother, and plurality of births have been shown. In addition to the recognized innate differences, improved knowledge of environmental factors, such as social status, health of the mother, and nutrition, promotes increasing recognition.

Data regarding average weights of live births, collected from UN, WHO, and other reports, give a range of values from 2,760 to 3,500 Gm. (6 to 7.75 lb.). Caucasians show the highest birth weights regardless of geographic location (Netherlands, 3,500 Gm. (7.75 lb.) [6]; Birmingham, England, 3,280 Gm. (7.25 lb.) [5]; United States (white population), 3,320 Gm. (7.35 lb.); and South Africa (European population), 3,390 Gm. (7.5 lb.).[7] In contrast, average weights below 3,000 Gm. (6.75 lb.) are almost consistently found in the Bantu populations of South Africa,[8] and similar figures are recorded in India [9] and Ceylon.[10]

A more accurate picture of the variation of birth weights is shown by the distribution of live births by weight, as in figure 7. Data for the white popu-

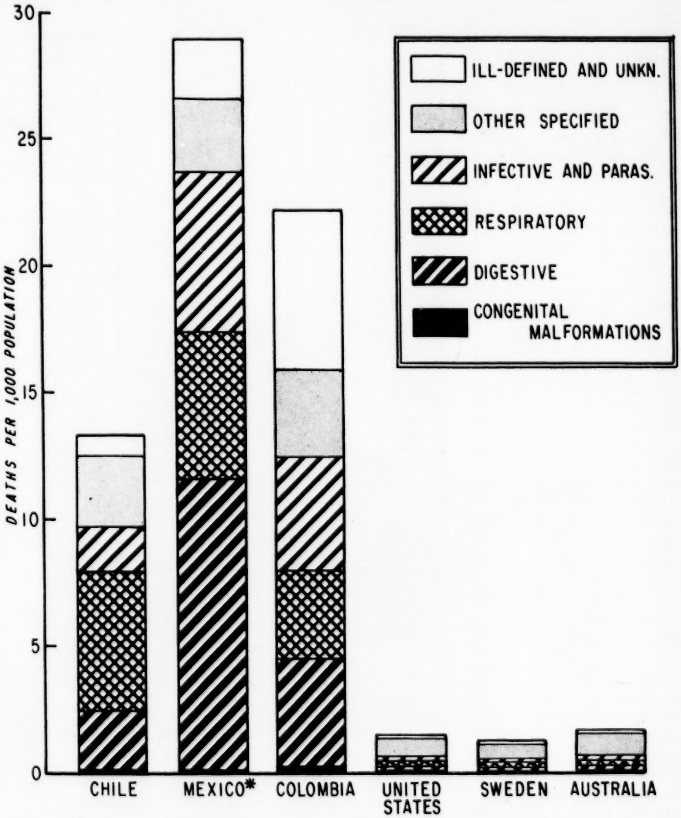

Fig. 4.—Deaths per 1,000 population by cause in age group 1-4 years for six selected countries, 1950-1952 average (for Mexico, calculation was based on 1950-1951 distribution of deaths).

lation of the United States (from special reports of the National Office of Vital Statistics) and for Birmingham, England,[5] show the same general weight distribution. The other racial groups have a shift to the left, that is, to lower weights. The Bantu of South Africa [7] and the nonwhite population in the United States have higher percentages

in the lower weight groups than do the Caucasians. The greatest shift to the left is shown by the Indians of South Africa [7] and of Calcutta.[9] (For the former group, data were collected from various hospitals and nursing homes in Durban, Pietermaritzburg, and Capetown. "Indian" is used to refer to persons from India or originating from India who have moved into the Union of South Africa. For the latter group, data were recorded in Ramkrishna Mission, Shishumangal Pratishthan, Calcutta, June, 1952, to February, 1954.) These differences in the weight distribution curves greatly influence the frequency of prematurity, taking the birth weight of 2,500 Gm. (5.5 lb.) as its upper limit according to the accepted classification.[11] Thus, for the United States and Birmingham, England, the proportions below this dividing line were 7.0% and 7.4% respectively. For the nonwhite population in the United States, the percentage was 11.2 and for the Bantu in South Africa 11.6. The percentages increased for the Indian in South Africa to 18.3 and for the group in Calcutta to 34.7. Taking into account, in addition, the low percentages of 3.5 for the Netherlands,[6] 4.6 for Denmark,[6] and 5.4 for Oslo, Norway,[12] where the average birth weights are known to be higher, the range in the frequencies of prematurity is very great. This raises questions about the adequacy of the dividing line of 2,500 Gm. as the upper limit for prematurity for all populations throughout the world.

Analysis of mortality by birth weight groups provides further evidence regarding the problem of measurement of prematurity by weight. Mortality in the first week of life (data from the National Office of Vital Statistics and Chaudhuri [9]) is shown in table 3 for three weight groups in Calcutta and in the white and nonwhite population of the United States. In Calcutta, where 35% of the births in the study weighed 2,500 Gm. or less and, thus, the average birth weight was low, 9.1% of the premature infants died under one week of age. The percentages of the premature infants who died under one week of age were much higher for the white population (16.2%) and for the nonwhite population (14.2%) of the United States, where only 7% of the white and

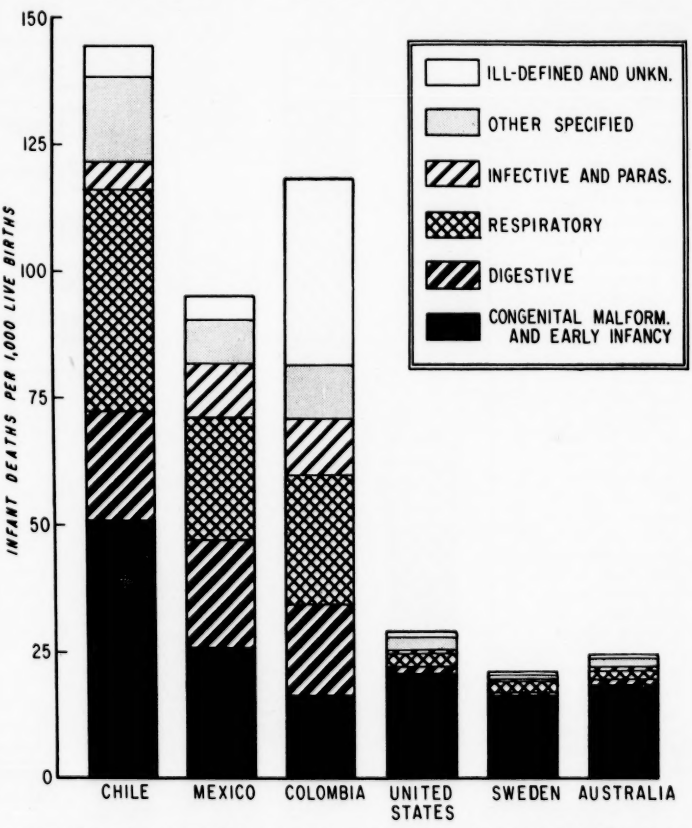

Fig. 5.—Infant deaths per 1,000 live births by cause for six selected countries, 1950-1952 average.

10% of the nonwhite live births were premature by the same standard. The average birth weight of the white live births in the United States was 3,320 Gm. (7.35 lb.) and of the nonwhite 3,270 Gm. (7.25 lb.). Thus, these data indicate that mortality is more favorable for premature infants by this definition equivalent to that of white infants, and in Calcutta [9] it is suggested that a lower maturity weight, 2,270 Gm. (5 lb.) be used.

Further study of the problems related to the definitions of immaturity by weight is needed, since they have implications for program planning. Only

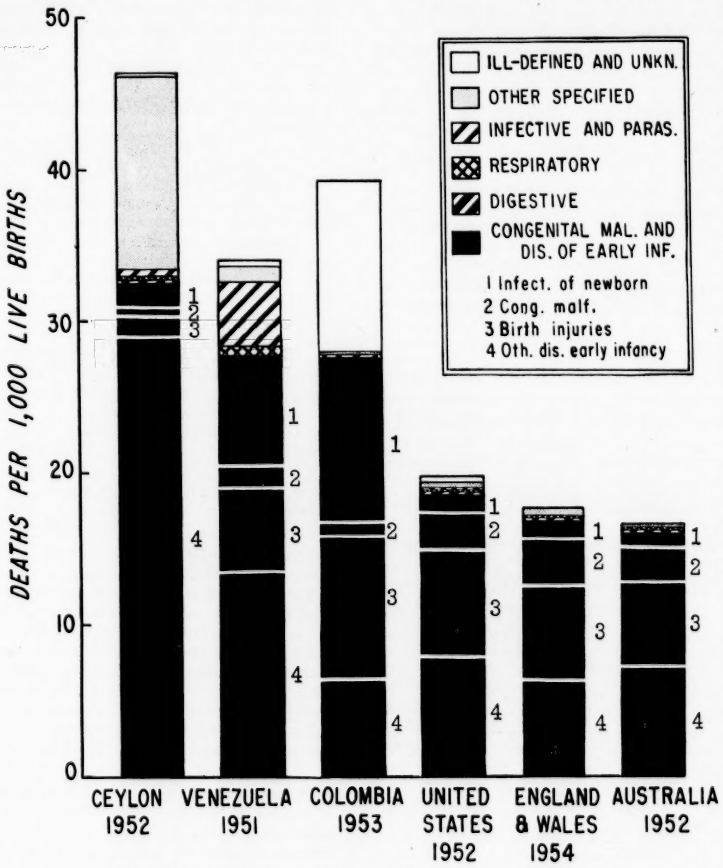

Fig. 6.—Neonatal deaths per 1,000 live births by cause for six selected countries.

in experiences with lower average birth weights. This indicates that, in populations with substantially different birth weights, the single limit of 2,500 Gm. cannot be utilized to compare physiological performance. In a study in Baltimore [13] of Negro infants it was necessary that the limit be lowered to 2,320 Gm. (5.25 lb.) to obtain a mortality rate differences within the same ethnic group allow us to infer that environmental circumstances influence the distribution of birth weights. The following evidence is suggestive. Van Gelderen, Posthuma, and De Haas [9] found that the average birth weight in the Netherlands has increased by approximately 250 Gm. (0.5 lb.) in the last 20 years. Data pre-

sented at the Second Inter-African Conference on Nutrition, Fajara, Gambia, 1952, showed consistently lower birth weights of infants born of mothers in nonpaying maternity wards than in paying wards.

TABLE 2.—*Fetal and Neonatal Deaths per 1,000 Births by Cause for Birmingham, England, 1952-1954* [5]

Cause of Death	Total	Fetal Deaths			Neonatal Deaths		
		Total	Premature	Mature	Total	Premature	Mature
All causes	38.8	22.7	16.1	21.8	12.0	9.7	17.0	10.7	6.3
Antenatal									
Toxemia	5.9	4.6	1.3	4.5	3.3	1.2	1.3	1.3	0.0
Separation of placenta	4.1	3.3	0.8	1.9	1.1	0.7	2.2	2.2	0.1
Other	4.0	2.3	1.7	2.4	1.3	1.1	1.6	1.0	0.6
Intranatal	7.5	2.2	5.2	4.9	1.3	2.6	2.6	1.0	1.6
Postnatal	2.3	0.8	1.5	...	...	...	2.3	0.8	1.5
Fetal abnormality	7.6	4.0	3.6	3.7	2.6	1.1	3.9	1.5	2.5
Prematurity and unknown	7.4	5.5	2.0	4.4	2.4	2.0	3.0	3.0	...

Within four racial groups in Malaya and Ceylon these differences varied from 130 to 410 Gm (0.25 to 1 lb.). For the Caucasian race, some displacement to lower birth weights was found in World War II in the Netherlands [14] and an extreme displacement to lower birth weights was found during the starvation period of the Leningrad siege in 1942.[15]

Mortality and Social Class

Finally, in a consideration of the role of the environment, there are obviously many social and economic factors determining the outcome

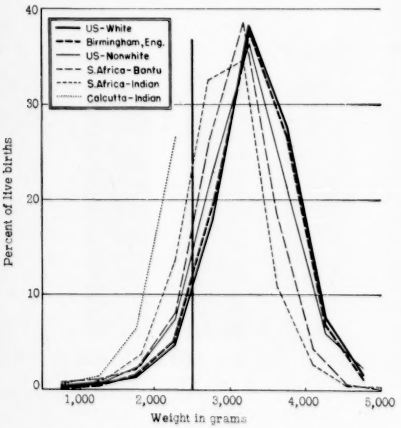

Fig. 7.—Percentage distribution of live births by weight in grams for six selected areas or groups.

of pregnancy, the condition of the child at birth, and his chances of survival. Utilizing the Registrar General's Decennial Supplement for England and Wales in 1951 [16] (fig. 8 and table 4), the mortality was lowest for the professional class, with a continuous increase to class 5. Furthermore, there was a difference in the increase in mortality in the three periods analyzed; from class 1 to class 5 the increase was 58% for fetal mortality, 72% for neonatal, and 278% for postneonatal mortality. The influence of social class can also be seen for various causes of infant mortality. In England and Wales in 1950, the death rate from pneumonia and gastroenteritis combined was five times as high in the unskilled as in the professional class, while the death rates from congenital malformations, birth injury, and asphyxia and atelectasis were less than twice as high in the unskilled as in the professional class.

Comment

In considering the challenge of fetal loss and infant mortality on a world-wide basis, the following general observations appear relevant. Sharp differences exist between technically developed and less developed areas. In the former areas, mortality has been considerably reduced in the age period 1-11 months and almost completely reduced in the

TABLE 3.—*Deaths Under One Week of Premature Infants, with Rates per 100 Live Births, According to Birth Weight for Calcutta* [9] *and for White and Nonwhite Population in the United States*

Weight, (Gm.)	Calcutta (Jan., 1953-Feb., 1954)			United States (Jan.-March, 1950)					
				White			Nonwhite		
	Live Births	Deaths Under 1 Wk.		Live Births	Deaths Under 1 Wk.		Live Births	Deaths Under 1 Wk.	
		No.	Rate		No.	Rate		No.	Rate
Total	2,271	208	9.1	49,934	8,092	16.2	11,703	1,663	14.2
1,500 or less	121	81	66.9	7,208	4,866	67.0	1,741	1,029	59.1
1,501-2,000	410	74	18.0	9,206	1,782	19.4	2,182	337	15.4
2,001-2,500	1,740	53	3.1	33,460	1,444	4.3	7,780	297	3.8

next age group, 1-4 years. In contrast, much smaller declines have occurred in neonatal mortality, and it can be assumed that the declines in fetal mortality have been of the same order. The reductions in neonatal mortality have been particularly small in the early neonatal period. This results in perinatal mortality assuming an increasingly greater importance and becoming the major problem of wastage of life in technically developed areas.

For the technically less developed areas, while the perinatal mortality rate is relatively higher than in the developed areas, the mortality in the age period after one month is considerable, and there is, in addition, excessive mortality in the pre-school-age period. Here the most important fraction of wastage in child life is in the period one month to 4 years. This has great importance in program planning, since the excessive mortality in infancy and in preschool age is essentially the result of causes strongly dependent on environmental conditions, namely, gastrointestinal, respiratory, infectious, and parasitic diseases and the underlying influence of malnutrition. These causes can almost entirely be eliminated through the development of

a health program that, besides supplying personal advice to the mother and the family, will aim at control of communicable diseases and improvement of basic sanitation and of nutrition; this is ultimately dependent on a broad program of socioeconomic

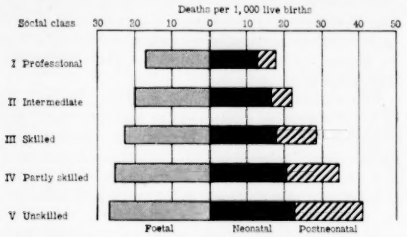

Fig. 8.—Fetal, neonatal, and postneonatal deaths per 1,000 live births by social class, England and Wales, 1950.

development. This is further corroborated by the selective effect of social class on fetal, neonatal, and postneonatal mortality, with the greatest reduction in postneonatal mortality, which is more strongly influenced by the environment. Although less evident, these same causes influence late neonatal mortality. Some specific causes, such as syphilis and tetanus of the newborn infant may unduly increase the early neonatal mortality. It has been reported that in many villages in rural China tetanus neonatorum caused from 15 to 20% of the deaths of newborn infants during the first month of life.[17] Where such diseases cause many deaths, their reduction through specific attack may then produce a marked decline in early neonatal mortality. There is, furthermore, evidence that poor nutrition plays a role in increasing fetal loss and prematurity and in lowering the birth weight of the mature infant.

There seem to be three phases of action for the solution to this problem. In less developed areas a first point of attack is to establish basic public health services, including maternal and child health and improvement of nutrition; this will have considerable influence on survival from conception to school age. Within this program, the introduction of some specific measures may produce good results even in unfavorable rural circumstances in less developed areas. Thus, emphasis on the need for prenatal supervision to all pregnant women, including treatment of important infectious diseases and correction of severe anemia and of poor nutrition, will lower fetal loss and prematurity and increase birth weights. Provision of limited facilities for delivery of difficult cases and emergencies and education of the village midwives to prevent malpractice will save many lives during and immediately after birth. Also, attack on diarrheal disease through specific measures and improvement of weaning diets by early introduction of proteins in the feeding, supplementary to breast-feeding, will save a tremendous number of lives in many areas of the world.

The next point of attack is the one that has been met partly by most of the technically advanced countries that have had well-improved health conditions for the past 15 years. These countries embarked on a series of specific measures of attack aiming at further reduction of maternal and infant mortality. The success of national programs, such as the Emergency Maternity and Infant Care Program (EMIC) in the United States and the program for improved nutrition and care of mothers and children in the United Kingdom, launched during World War II, has been the result of efficient program planning and development, concomitant with fuller employment and increased family income.

Rapid declines led to recognition of the need for emphasis on the perinatal period and for team approach, with full integration of obstetric, pediatric and nursing skills, through the prenatal, natal, and postnatal periods which require highly specialized techniques in care. Further declines in perinatal mortality have resulted in rates below those that only a few years ago were considered irreducible. Thus, in limited groups,[3] under highly favorable circumstances, perinatal mortality has been reduced to 20 per 1,000 births, with approximately one-half in late fetal and one-half in early neonatal life. However, national mortality figures for advanced countries remain between 30 and 40 per 1,000 births, and the reduction to 20 per 1,000 will represent considerable financial and professional effort which may at present be beyond the possibilities even of some highly developed countries.

Today, increasing numbers of children with handicaps from fetal abnormality, prematurity, and birth injury can be saved. Official and private efforts for medical, educational, and social rehabilitation of handicapped children have made it possible

TABLE 4.—*Fetal, Neonatal, and Postneonatal Deaths per 1,000 Live Births by Social Class, England and Wales, 1950* [16]

Social Class	Fetal	Neonatal (under 4 Wk.)	Postneonatal (4 Wk.-1 Yr.)
All classes	23.1	18.5	11.3
1. Professional	17.0	12.9	5.0
2. Intermediate	20.0	16.4	6.1
3. Skilled	22.6	17.9	10.6
4. Partly skilled	25.3	20.5	14.0
5. Unskilled	26.8	22.2	18.9

for them to achieve their highest potentiality and to be fully integrated in their community. Yet, emphasis on prevention is justified, since the process of rehabilitation is almost invariably costly and even a slight residual handicap curtails opportunity for fullest development.

Until fairly recently, congenital abnormalities were believed to be essentially the result of innate factors. But ever since maternal rubella was proved to influence the development of congenital abnormalities, this belief has been under constant attack. Today, newer knowledge points to the influence of environmental factors on the development of malformations and other handicaps. Mothers of children with cerebral palsy, epilepsy, mental subnormality, and behavior disorders have been found in a study to have had complications during pregnancy and childbirth more frequently than did mothers of normal children.[18] Since these complications also result in increased fetal loss and prematurity, a continuum of reproductive casualty with lethal and sublethal effects is suggested.

The concept of perinatal hazards, while limited to a narrow time period in terms of mortality, is considerably broadened by the recognition that they result from unfavorable circumstances in pregnancy and in early life of the mother and that their effect may be felt through a handicapped condition necessitating special care and attention throughout life.

No doubt, improved methods of care will continue to be part of a program aiming at the reduction of perinatal mortality. However, the future points to the value of a broad program of research for preventive action that might eventually break the vicious circle between the unfavorable preconceptional and prenatal circumstances and their effect on the offspring. If successful, this program, as a last and newer point of attack, should greatly influence the situation in countries with present low infant mortality rates and may also benefit the less developed areas. Present programs with emphasis on medical care have limited possibilities in these latter areas for lack of both the great financial expenditures and the highly specialized professional skills and facilities which they require. But if, through future knowledge resulting from research, more easily applicable preventive measures are made available, these could become part of the broad program of development of health services. These measures may then result in more effective prevention of fetal loss and greater saving of lives in early infancy, even in economically less developed areas.

Summary

Data on fetal loss, prematurity, and infant mortality on a world basis, within the over-all picture of mortality in childhood throughout the world, point up the excessive mortality still prevailing in economically less developed areas in the age groups of 1-11 months and 1-4 years and the great reduction of mortality in those same age groups in the technically developed countries. This reduction places the major problem of mortality in childhood in these latter countries in the perinatal period. The causes of fetal loss and neonatal mortality are interrelated, and there is a need for a definition of perinatal mortality that allows comparison of data from countries with greatly different conditions. In addition, taking account of the importance of prematurity in relation to perinatal mortality, the use of the present definition of prematurity, based on weight, creates problems when countries, areas, or groups with different birth weight distribution curves are analyzed.

For reduction of perinatal mortality, a first attack on excessive postneonatal and preschool-age mortality may be made through the development of adequate general public health and maternal and child health services. These may considerably reduce mortality in those age groups and will also, to some extent, affect neonatal and, therefore, perinatal mortality. Such programs as premature infant care and rehabilitation of handicapping conditions have achieved considerable reduction in infant mortality rates in some countries. However, an intensive program of research for the prevention of those conditions that determine the size of perinatal mortality rates appears, at present, necessary. The discovery of adequate preventive measures not only would allow further reduction of the perinatal problem in highly developed countries but might prove more generally applicable in technically less developed areas than programs of specialized care which are too costly and require too highly specialized skills and facilities to have any real effect within the low priority for program planning that can be given them at the present time.

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THE TREATMENT OF PSORIASIS AND OTHER DERMATOSES WITH TRIAMCINOLONE (ARISTOCORT)

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958
167

Sixty patients with psoriasis were treated with triamcinolone, a corticosteroid, in doses of 12 to 16 mg. daily by mouth. In 36 of the patients the response was prompt and unquestionable; within a week, the scaling and erythema diminished significantly, and within two to four weeks of continued adequate dosage the psoriasis was, in some patients, completely erased. Upon cessation of treatment or reduction of dosage, however, the lesions regularly returned. The remaining 24 patients failed to show any response. A wide variety of reversible side-effects were observed. Some were favorable, such as the stimulation of hair-growth in alopecia areata, and many were unfavorable, such as flushing, hyperhidrosis, facial hirsutism, and facial contour changes. Triamcinolone was found to be highly antiallergic, antirheumatic, and antiinflammatory, and therefore useful in a variety of dermatitides; its use in psoriasis should probably be limited to acute extending cases not controllable by other means or to very extensive and severe chronic forms.

Psoriasis is a common chronic scaling skin disease which has long defied all attempts to determine a specific cause or treatment. It appears as a recurrent hereditary reaction pattern to a wide variety of known, as well as unknown, trauma.[1] Its course is capricious. Its severity may range from an insignificant pitting of the nails to a fatal exfoliative dermatitis. Treatment programs include an extremely large number of topical as well as systemic measures. None of these can be considered uniformly effective or in any way specific.

Accordingly, when Hollander and others [2] acquainted us with their finding that the new corticosteroid, triamcinolone (Aristocort), had a marked therapeutic effect on psoriasis, we immediately undertook an investigation of the effects of this new fluoroprednisolone compound (fig. 1). The present report details our findings over the year prior to writing in the treatment of 60 patients with psoriasis and 70 patients with assorted dermatological problems other than psoriasis. The initial patient has been treated for 10 months, and this report cannot, therefore, present an estimate of the long-term effectiveness and toxicity of triamcinolone.

Material

The present data are derived from direct personal observations on 130 consecutive patients, 60 with clinically identifiable psoriasis and 70 with inflammatory dermatoses. No attempt was made to select specific patients. All forms, types, and degrees of psoriasis were included for a more accurate estimate of the actual spectrum of action of triamcinolone. The 70 patients with inflammatory dermatoses were studied for base-line data on the

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relative corticosteroid activity of this compound. Rigid control data are lacking, since placebo therapy was not employed. However, only rapid unquestionable therapeutic effects were viewed as resulting from triamcinolone therapy. The minor, slight, or questionable benefits are ignored from the standpoint of evaluation.

The dosage of triamcinolone varied from 4 to 32 mg. orally each day. In the earliest phases of the study, triamcinolone diacetate was administered, but the majority of the observations refer to the free alcohol. No difference in response to these two forms could be perceived by us. Low, rather than high, dosage was often employed, in part because of the scarcity of the drug early in the study, the necessity of using caution in the early phases of any evaluation, and the relative insignificance of the clinical manifestations in some instances. Local treatment was usually interdicted.

In selected instances 0.5 and 1.0% triamcinolone cream and ointment were employed, with a blind paired control method of assay. In many of the

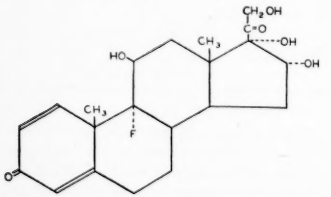

Fig. 1.—Structural formula of triamcinolone (Aristocort). It can be characterized as 9α-fluoro-16α-hydroxyΔ^1-hydrocortisone.

patients the local effect of triamcinolone was ascertained by means of a skin test consisting of the injection into the lesion of 0.05 ml. of a sterile 1% suspension of triamcinolone in isotonic sodium chloride solution. This is the assay technique advocated by Goldman and others.[3]

Results

Table 1 outlines the results obtained in the treatment of psoriasis, whereas table 2 summarizes the clinical effectiveness of triamcinolone in the treatment of some common inflammatory skin changes in which steroids have been widely recognized to be of value. It is significant to note in table 1 that triamcinolone had a prompt temporary clearing effect on as many as 60% of the patients presenting psoriasis. Furthermore, in table 2, triamcinolone is seen to be an effective anti-inflammatory glucocorticoid in a relatively small dosage.

The response of psoriasis which we have observed in the 36 of 60 patients treated was a rapid unquestionable one. Within one week the scaling and erythema had diminished significantly, and with a continued adequate dosage the psoriasis was in some patients completely erased in two to four weeks. Only residual pigmentary macular changes remained at the sites of previously scaly hyperkeratotic chronic plaques of psoriasis. Psoriasis of all areas—the palms, groin, scalp, knees, and elsewhere—fled in the responsive patient. Indeed, in long-term therapy we have seen psoriatic nails return to normal.

Triamcinolone has not been recorded by us as effective in any instance in which the morbidostatic changes were less than impressive. Quasi-improvement or delayed improvement has not been interpreted as due to the drug. The second aspect of the response which is of considerable importance is the fact that it is almost invariably reversible. Upon cessation of treatment or reduction of the dosage below the maintenance level, the psoriatic lesions have regularly returned, sometimes in more aggravated form. Within a week of withdrawal of triamcinolone, clinical evidence of psoriasis reappears or increased scaling and erythema become evident.

A full 40% of the 60 patients with psoriasis failed to show any response. What characterized this group? We could see no distinguishing feature on the basis of clinical appearance, location, or duration of lesions or the age or sex of the patient. In part, however, this nonreactive group was made up of those with recalcitrant intractable chronic psoriasis, patients who failed to respond to numerous other modalities such as ultraviolet light and tar. Most significantly, however, our studies indicated that these patients were refractory to the local effect of triamcinolone. Twenty-one patients of the group with psoriasis were skin-tested with 1% triamcinolone suspension. In each of nine patients failing to respond to triamcinolone given orally, the skin test also failed to produce a local response. In marked contrast, in each of the 12 patients showing a response to triamcinolone given orally, the skin tests showed a sharply circumscribed area of complete involution at the site of the triamcinolone skin test (fig. 2). The positive skin-test responses (fig. 3) occurred within 48 to 72 hours and persisted for weeks. Control skin tests with saline solution were without effect, although it is well known that local injection of hydrocortisone acetate may cause local involution of psoriasis.[3]

Psoriasis is far more of a reaction pattern than a disease sui generis. The Koebner phenomenon reflects the multiplicity of causes for psoriasis. We feel these multiple causative factors for psoriasis suggest why triamcinolone is not regularly effective. It appears that possibly triamcinolone is effective in suppressive allergic factors which trigger psoriasis in certain people. Still again seborrheic dermatitis responds so well to the compound (table 2) that one might suspect that seborrheic psoriasis may form the bulk of the examples involuting under steroid management. However, we

TABLE 1.—*Results of Triamcinolone Therapy in Treatment of Psoriasis*

Case No.	Sex	Age, Yr.	Duration of Clinical Psoriasis, Yr.	Distribution	Daily Dosage (Mg.) of Triamcinolone: Maximum	Daily Dosage (Mg.) of Triamcinolone: Maintenance	Observation Period, Mo.	Side-effects	Clinical Result	Skin Test
1	F	39	29	Generalized	12	...	1	None	Effective	...
2	M	52	5	Scalp, ears, nose, gluteal cleft, scrotum, penis	6	4	5	None	Effective	...
3	F	48	1	Hands, elbow, localized	6	...	1¾	Ulcer, duodenal	Effective	...
4	F	29	2	Upper and lower extremities, extending	16	...	½	None	No effect	...
5	M	45	9	Right foot, ankle	6	6	1½	None	Effective	...
6	F	60	5½	Generalized	16	12	¾	None	Effective	...
7	F	27	17	Generalized	18	...	1½	None	No effect	No effect
8	F	8	1	Generalized	8	4	2	None	No effect	...
9	M	78	1½	Left foot	6	2	3	None	No effect	...
10	M	49	15	Legs, sacrum, abdomen, nails	10	6	2	None	Effective	Effective
11	F	45	10	Generalized	16	12	1½	Cushing-like changes	Effective	Effective
12	M	63	3	Generalized	8	2	2	None	Effective	...
13	F	42	7	Generalized	16	...	1	Cushing-like changes	Effective	Effective
14	F	42	8 mo.	Hands	10	4	1	None	Effective	...
15	F	50	4	Elbows, knees, legs	4	1	2	None	No effect	...
16	M	41	15	Generalized	16	12	3	None	No effect	...
17	M	58	7 mo.	Scalp, face, chest, extending	8	...	6	None	Effective	...
18	F	19	6	Generalized	14	8	8	Dizziness, hirsutism	Effective	Effective
19	F	12	10	Hands, feet, extremities, extending	8	8	2	None	Effective	...
20	F	44	23	Generalized	12	...	½	None	No effect	...
21	F	51	10	Face, vulva, hands	8	4	4½	None	Effective	...
22	M	41	11	Scalp, elbows, umbilicus, penis	6	4	1	None	Effective	...
23	M	64	10	Elbows, legs, abdomen, extending	16	8	4	None	Effective	...
24	M	73	20	Chest, abdomen, back, extremities extending	16	8	2	Weakness, leg cramps	No effect	No effect
25	M	52	2½	Scalp, ears, trunk, elbows, inguinal region, nails, extending	18	4	2	None	No effect	...
26	F	52	8	Generalized	20	8	3	Cushing-like changes	No effect	No effect
27	F	42	25	Generalized	20	12	6	None	No effect	No effect
28	F	78	7	Scalp, chest, abdomen	6	...	½	None	No effect	No effect
29	F	52	8	Hands	6	2	5	None	Effective	...
30	F	24	7	Scalp, ears, face, elbows, knees, abdomen, lumbosacral and gluteal region	10	8	1½	None	Effective	Effective
31	F	57	20	Plantar surfaces of feet	12	...	¼	None	Effective	...
32	M	51	1	Hands, heels	8	6	5	None	Effective	...
33	F	57	2½	Abdomen, scalp, back, extremities, extending	12	6	7	Dizziness, Cushing-like changes	No effect	...
34	M	52	24	Thighs, sacral area, new attack	12	...	1	None	Effective	Effective
35	M	59	3	Scalp, elbows, knees, gluteal cleft	10	...	2	None	Effective	...
36	M	30	1	Fingers, nails	8	...	¾	Abdominal pain	Effective	...
37	M	39	6 mo.	Scalp, face, knees	12	...	5	None	No effect	No effect
38	F	40	15	Generalized	32	8	4	None	Effective	Effective
39	F	54	5	Scalp, chest, thighs, nails, extending	8	2	8	None	Effective	Effective
40	F	58	3	Scalp, chest, inguinal region, ears, extending	12	...	¼	None	Effective	...
41	F	21	7	Generalized	12	12	7	None	Effective	Effective
42	F	24	1	Legs	12	...	1	None	No effect	...
43	M	45	3	Generalized	8	...		Gastric ulcer, pain	Effective	Effective
44	M	74	20	Hands, forearms, neck, umbilicus, inguinal region, buttocks, extending	6	...	7	Weakness	Effective	...
45	F	28	15	Generalized	16	4	1½	None	Effective	...
46	F	55	1	Ears, scalp	6	...	2	None	No effect	...
47	F	51	1	Scalp	4	...	½	None	No effect	...
48	F	59	3	Nails, elbow	4	...	2	None	No effect	...
49	F	23	3	Scalp, chest, inguinal region, gluteal region, knees, elbows, extending	12	12	1½	None	Effective	Effective
50	F	6 mo.	4 mo.	Scalp, eyelids, neck, abdomen, inguinal region, back	8	...	2	None	No effect	...
51	F	48	26	Knees, elbows	12	12	4	None	Effective	...
52	M	10	6	Generalized	8	...	2	None	No effect	...
53	F	41	1	Generalized	10	6	2	None	Effective	...
54	F	43	1½	Hands, nails	8	...	2	None	Effective	No effect
55	M	57	12	Knees, hands, feet	12	...	¾	None	No effect	...
56	F	43	28	Generalized	16	...	½	None	No effect	No effect
57	F	48	9	Scalp, arms, back, abdomen, legs, extending	16	...	1	None	No effect	No effect
58	F	48	10	Legs	8	...	½	Febrile reaction	No effect	...
59	F	54	2½	Hands, feet	8	6	6	None	Effective	...
60	M	53	10	Generalized	16	12	2	None	Effective	Effective

have seen classic seborrheic psoriasis fail to respond to triamcinolone. Further studies are now in progress to determine the possible prognostic value of biopsy findings. Our early impression is that an eczematoid histological cast to the psoriasis patterning is correlated with triamcinolone responsiveness.

The dosage of triamcinolone employed with success most commonly was 4 mg. orally four times a day. Dosage higher than this did not seem to lead to significantly higher improvement rates. Dosage below this may not give maximal results. Nevertheless, we have seen a number of patients respond to 8 mg. per day. The maintenance dosage is ascer-

tained after the psoriasis is 90% cleared. Gradual tapering of the level is as critical here as with the other steroids. We commonly were unable to reduce the triamcinolone maintenance level below 8 mg. per day. At times the maintenance level would fluctuate. In a few patients use of the drug was unavoidably stopped suddenly due to an interruption in supplies. A sharp recurrence of the psoriasis was noted, and on occasion this proved to be strangely refractory to resumed triamcinolone therapy.

TABLE 2.—*Summary of Clinical Effects of Triamcinolone, 4 to 16 Mg. per Day, on Dermatoses Other Than Psoriasis in Fifty-one Patients**

Type of Lesion	Helped, No.	Not Helped, No.
Chronic eczematous eruptions, including atopy	14	5
Localized neurodermatitis	4	2
Contact dermatitis	6	6
Seborrheic dermatitis	9	0
Alopecia areata	4	1

* Data on nineteen other patients presenting miscellaneous eruptions are excluded because of paucity of experience in any one category.

It was with considerable disappointment that we found that 0.5 and 1.0% topical triamcinolone creams and ointments were regularly without any distinctive benefit on psoriasis. It is to be assumed that permeability factors here prevent absorption of adequate amounts, since injected triamcinolone is effective locally.

Side-effects

Side-effects of systemic triamcinolone therapy in the dosage employed by us were similar to those seen with other corticosteroids. Two patients showed a reactivation of duodenal ulcer during triamcinolone therapy. However, we found no evidence of hypertension, edema, or hyperglycemia. In five patients distinct Cushing-like changes developed—moon face, buffalo humping, and hirsutism. Hirsutism was seen as an isolated finding in an additional four patients. We feel that triamcinolone has a greater hair-growth stimulating effect than the other steroids in use. These side-effects were reversible upon stopping the therapy. An occasional patient complained of epigastric distress, pyrosis, and nausea following triamcinolone dosage. This could be corrected by the simultaneous administration of an antacid. Constipation was noted by two patients. One patient complained of palpitations, tremor, and weakness after taking each triamcinolone tablet. Another developed marked leg cramps. One patient noted a metallic taste in the mouth.

The strangest finding, seen in two patients, was the development of intense generalized flushing and hyperhidrosis about 30 to 45 minutes after a tablet of triamcinolone had been taken. In three patients, purpura developed during the triamcinolone therapy. Three patients had attacks of vertigo and fainting. In addition, one patient experienced three convulsive attacks. No direct relationship could be ascertained, but it was noted that one year prior to steroid therapy this patient had had a convulsive attack. An electrocardiogram at that time revealed no evidence of epilepsy. A number of patients showed an increase in appetite. No psychic disturbances were noted. Finally, it was gratifying to have a steroid compound which did not lead to fluid retention and edema. Indeed, several patients experienced mild diuresis and disappearance of chronic leg edema when they began triamcinolone therapy.

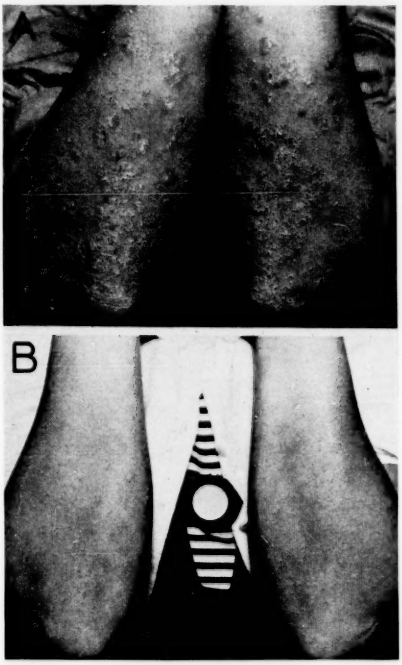

Fig. 2 (case 11).—*A*, view of psoriasis of elbows before triamcinolone treatment. These lesions had been present for many years and had failed to respond to previous local and systemic medication. *B*, view of same area after two weeks of treatment with triamcinolone in a dosage of 4 mg. three times daily. No local treatment was used.

All patients have been closely observed, and in no instance has the drug been indiscriminately prescribed. Much remains to be observed regarding the long-term effects of steroids on man.

Comment

Rein and others [4] have published their findings on the relative potency of prednisolone and triamcinolone in the treatment of skin disease. They viewed triamcinolone as significantly more effective than prednisolone. Sherwood and Cooke,[5] in studies on asthma and rhinitis, found triamcinolone twice as active as prednisone and prednisolone on an equal weight basis. Our own limited studies suggest that, although variable results may be expected in any given patient, 4 mg. of triamcinolone may be equivalent to as much as 10 mg. of prednisolone in the treatment of the dermatitides. We have seen an occasional patient in whom prednisolone was more effective than triamcinolone. In others, they appear equivalent on a weight basis.

Triamcinolone is a corticosteroid developed in a search for corticoid analogues which might be expected to have a lower incidence of serious side-effects.[6] As a fluoro-derivative of prednisolone, it has proved to be a highly effective antiallergic, antirheumatic, anti-inflammatory compound. We have asked ourselves if the action of triamcinolone on certain examples of psoriasis is a distinctive new pharmacodynamic effect or whether it reflects the well-known anti-inflammatory action of steroids. We are inclined to view the triamcinolone action as steroidal and, as such, a nondistinctive anti-inflammatory action. We have found that, although nonerythrodermic psoriasis is refractory to the usual clinical dosage of steroids, it is possible to suppress many examples by massive doses of hydrocortisone (100 mg. per day). This is in agreement with previous reports.[7] We would view use of triamcinolone as an extension of this form of therapy. Triamcinolone presumably achieves an anti-inflammatory level in the skin, which could previously be attained only by giving steroids in very large dosage. Such dosage invariably led to toxic side-effects necessitating discontinuance. It now appears that at least some of the patients with chronic severe psoriasis can be given temporary assistance without fear of severe side-effects.

Triamcinolone in common with all other anti-psoriasis remedies is no cure for psoriasis. It must be recognized as purely palliative. Its use must reflect this fact. Furthermore, the physician should use it solely in an attempt to combat the severe and the generalized forms of the disease. Triamcinolone is a strong corticosteroid with influences throughout the entire body. It is not to be given for relief from a few scales on the elbows.

Triamcinolone proved to be remarkably effective in the treatment of alopecia areata. This compound seems to have a specific stimulant effect on hair growth, since hirsutism was a prominent side-effect in a number of our patients. Unfortunately, topical triamcinolone therapy proved to be without effect in the treatment of patches of alopecia areata.

In the patients in whom comparative studies could be made, it appeared that 4 mg. of triamcinolone was often equivalent to as much as 10 mg. of prednisolone in the treatment of inflammatory dermatoses. However, this was not an invariable finding, for in a few patients prednisolone proved more effective than triamcinolone when given in equal amounts. Certainly the indications for triamcinolone are the same as for the other steroids. Exfoliative dermatitis, pemphigus vulgaris, and scleroderma are other examples of disease, not shown in table 2, which responded to triamcinolone.

Summary

Triamcinolone, a new fluoroprednisolone compound, has been shown to have a significant temporary suppressive effect on psoriasis. Thirty-six of a series of 60 consecutive patients with psoriasis proved to respond rapidly and dramatically to from 12 to 16 mg. of triamcinolone daily. This group presented the distinctive finding of local involution of psoriasis at the site of injection of triamcinolone intradermally. Relapses invariably occurred when the triamcinolone therapy was withheld. Topical triamcinolone therapy was without effect in the treatment of psoriatic lesions.

In view of the rapid relapse which has invariably been noted following suspension of triamcinolone therapy for psoriasis, it seems probable that reduction of the dose to zero will offer great difficulty in many patients. On the basis of our experience to date, we have adopted an attitude of considerable conservatism in initiating such therapy, reserving it only for acute extending psoriasis not controllable by other means or for very extensive and severe chronic psoriasis. Triamcinolone also proved to have potent anti-inflammatory properties in the treatment of various other dermatitides.

Fig. 3 (case 39).—Close-up view of psoriatic plaque showing small central clearing at exact site of intradermal injection of 1% triamcinolone suspension one week previously.

3400 Spruce St. (4) (Dr. Shelley).

The triamcinolone used in this study was supplied as Aristocort, in both tablet and topical forms, by Dr. Christopher H. Demos of the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

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STATIC AND DYNAMIC ELECTROCARDIOGRAPHIC PHENOMENA IN CORONARY ARTERY DISEASE

Harold D. Levine, M.D., Boston

The point of view is stressed that the electrocardiogram must be interpreted in terms of whether its appearance is fixed or changing. A limited number of serial electrocardiograms generally permits decision regarding the reversibility or nonreversibility of the electrocardiographic alterations. Two case histories illustrate the occasional disappearance of characteristic electrocardiographic changes of myocardial infarction. It is emphasized that the electrocardiogram as such is not generally helpful in demonstrating the extension of an acute myocardial infarct and that once a diagnosis of acute infarction has been settled on the basis of dynamic sequential changes, there is no good reason for indiscriminate repetition of the electrocardiogram.

From time to time many serious workers in electrocardiography have come to the conclusion that this soil has been so thoroughly worked over that the yield from further tillage will be negligible. Sir Thomas Lewis, for example, in about 1925, dissuaded Craib, a most brilliant and promising investigator, from further efforts in the field. Though electrocardiography is still largely empirical, attempts have been made, not entirely successfully, to change electrocardiography into a well-organized systematic and rational science. Some of the renaissance of interest in this subject has indeed come about through contact with the disciplines of biochemistry and biophysics. The important, large-scale, and continuing study of the electrocardiographic effects of various disturbances in electrolyte balance was sparked off by Winkler, and during the past few years Prinzmetal has undertaken a wholesale reexamination of the entire concept of electrical activation of the ventricular wall. The reawakened interest in electrocardiography would indicate that, as a tool of investigation, it has more than mere historical interest. The fundamental reason for this revival is a practical one, namely, the fact that the electrocardiogram, though limited in its scope, remains the most sensitive indicator of coronary artery disease, the most prevalent form of heart disease. It is estimated that there are from 15,000 to 20,000 electrocardiographs in current use in the United States. These facts justify and explain the continuing and increasing interest in the scientific and practical implications of the electrocardiogram.

The diagnosis of acute myocardial infarction may be made with reasonable accuracy on the basis of three electrocardiographic developments occurring more or less concurrently during a suspected clinical episode. These consist of sequential changes in the T wave, in the RS-T segment, and in the QRS complex. The diagnosis of old myocardial infarc-

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Read before the New Haven Medical Association, New Haven, Conn., Oct. 16, 1957.

tion, on the other hand, is generally made on the basis of fixed changes in the QRS complex alone. The electrocardiographic representation of myocardial impairment is epitomized in the general lability of the T wave of the electrocardiogram, the transience of the RS-T interval shifts, and the permanence of the QRS complex changes. This discussion concerns certain dynamic sequences and static appearances which in some cases may have theoretical significance as well as practical clinical meaning in the diagnosis of coronary artery disease.

Three Degrees of Myocardial Impairment

It is generally accepted that the T wave, as recorded at an electrode in relation to the epicardial surface of the left ventricle, would be expected to be inverted if the left ventricular myocardium throughout its entire thickness were of uniform physiological property and the process of electrical invasion and retreat each proceeded in orderly sequence from endocardium to epicardium. It is probably because electrical retreat, or repolarization, proceeds, rather, from epicardium to endocardium that the T wave is upright in the normal heart. This has been attributed to the longer duration of the excited state in the subendocardial than in the subepicardial layers of the ventricular wall. But this T wave, and presumably the conditions responsible for it, can be altered very readily and by a host of conditions.[1] For example, experimental cooling of the epicardial aspect of the ventricle can prolong the duration of the excited state in the subepicardium so that it equals that in the subendocardium, and the T wave, in consequence, becomes inverted. This same phenomenon can be observed in man. Drinking ice water and thus cooling the posteroinferior surface of the heart may invert the T waves in leads 2, 3, and aVF. The T-wave change is transient and disappears with removal of its cause. These thermal changes are the prototype of a mild injury to the myocardium. It needs to be emphasized that these changes are the result of intramyocardial alterations not necessarily dependent on the state of arterial perfusion of heart muscle. The experienced electrocardiographer has a whole catalogue of factors which affect the stability of the T wave. Numerous publications give voluminous testimony to this fact.

A more severe grade of injury results from the application of potassium solution to an excitable cell, tissue, or organ. Most of our information about this phenomenon has been furnished by the neurophysiologist. Potassium induces a local change in the transmembrane electrical potential, thus giving rise to a constant "current of injury." An electrode in relation to the epicardium of the left ventricle records an elevation of the RS-T segment when this injury is subepicardial in location, a depression of the RS-T segment when subendocardial. The effects of potassium represent the prototype of a more severe grade of injury than that imposed by local cooling or chilling. The RS-T segment elevation may be recorded at a precordial electrode in acute pericarditis, in acute myocarditis, in acute subepicardial, intramural, or transmural infarction, and, occasionally, for reasons unknown, as a perfectly normal variation. Nahum and Hoff[2] suggested long ago that electrical events in the subendocardium contribute little to the configuration of the electrocardiogram. This idea has recently been reformulated by Prinzmetal.[3] Perhaps this explains why in transmural infarction the RS-T segment depression which might develop in consequence of subendocardial injury is more than swamped out by the RS-T segment elevation which is attributable to the subepicardial injury.

The most severe grade of injury to the myocardium is actual death of myocardium. This process produces changes in the QRS complex which are generally irreversible. There are contradictory views regarding the origin of the QRS changes. The observations of Wilson underlie the traditional teaching of present-day electrocardiography. His observations indicate that, when an electrode which is insulated except at its tip is thrust through the ventricular wall, it records a sequence of changes as it is progressively withdrawn from endocardium to epicardium—at first, an entirely downward QS deflection at the endocardium, then a small R and deep S wave as the electrode is withdrawn into the subendocardial laminae of the ventricular wall, then equiphasic RS complexes about midway from endocardium to epicardium, then larger R and smaller S waves as it is drawn closer to the epicardium, and, finally, an entirely upright R wave at the epicardium. The translation from an endocardial QS to an epicardial R wave is predicated on the intermediation of healthy excitable myocardium. If this muscular wall is no longer excitable, the cavity QS potential is transmitted passively to the epicardium through this dead core of muscle which, though not excitable, transmits the impulse unchanged just as do other nonexcitable tissues, such as lung, bone, and liver. The cavity QS depends on outward activation of healthy ventricular myocardium elsewhere. Where the entire thickness of the ventricular wall is involved, an electrode in relation to the overlying epicardium should record a QS deflection; where a subendocardial wedge is infarcted, QR complexes should be recorded and the R wave should have a lower than original amplitude. According to Prinzmetal,[3] on the other hand, with a similar plunge electrode QS complexes are recorded in the inner three-fourths or so of the ventricular wall and the progressive build-up of more and more R wave and less and less S wave does not begin until the outer shell is reached.

Two sets of clinical observations at the Peter Bent Brigham Hospital seem to lend some support to Prinzmetal's experimental findings. The first con-

cerns observations in pure subendocardial infarction. The following case report may be regarded as typical of my experience with this group.

The patient had a classic clinical episode, including fever, fall in blood pressure, and elevation of the white blood cell count and sedimentation rate. The RS-T segment was generally depressed. As such, this is the unusual direction of the RS-T segment shift; hence, it is referred to as an "injury against the rule." No Q wave was recorded in these leads. Postmortem examination showed a ring-like subendocardial infarct.

If the traditional view of ventricular activation is correct, one would expect QR deflections over the epicardium in subendocardial infarction. If, on the other hand, the newer concepts are sound, infarction of the inner few millimeters of the ventricular wall should have no influence on the direction of the initial ventricular complex. Since this R wave is written by the outer shell of the myocardium, inactivation of the inner shell would not be expected to affect it. Thus, one would not expect Q waves at the epicardial electrode in subendocardial infarction. In my experience with subendocardial infarction, as verified at autopsy,[4] RS, not QR, deflections were recorded in association with RS-T segment depressions.

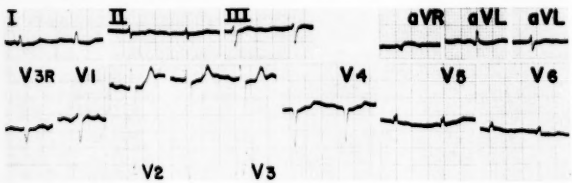

Fig. 1.—Electrocardiograms from 15-year-old boy with chronic myocarditis, proved subsequently at autopsy. Note QS complex in lead V_4. In older individual this change would almost certainly have been interpreted as indicating old anterior myocardial infarct.

The second set of experiences possibly bearing on the contention regarding the mode of activation of the ventricular wall concerns the electrocardiographic findings in constrictive pericarditis. During the past few years, experience at the Peter Bent Brigham Hospital in documented constrictive pericarditis has revealed an amazing and even disconcerting incidence of QR or QS complexes and with it the implication of actual myocardial damage. Among 26 cases, there were 4 in which an unequivocal diagnosis of old myocardial infarction was made on the basis of the electrocardiogram, 8 in which the electrocardiographic findings were in line with but not diagnostic of old myocardial infarction, and 14 in which no electrocardiographic evidence of infarction was seen. Pathological experience derived from a number of surgical specimens and two postmortem examinations has suggested that there is a pronounced intramyocardial extension of the epicardial eschar. Although the evidence is incomplete, these findings suggest that the present experience may be reconciled with Prinzmetal's concept of free wall activation. The layer of damaged myocardium extends through the outer into the inner shell of the myocardium from which QS deflections are recorded.

It is well known, incidentally, that electrocardiographic changes quite characteristic of old myocardial infarction may be induced by a number of processes resulting in scarring of the myocardium, e. g., scleroderma, amyloid disease, hemochromatosis, and the like.[1] The electrocardiogram is unable to discriminate between the fibrosis produced as the result of vascular disease and that due to these other processes. Figure 1 shows tracings recorded from a 15-year-old boy with chronic congestive heart failure of undetermined etiology. Note the QS deflections in lead V_4. This is the sort of change which in an older individual would suggest old anterior infarct. Postmortem examination showed chronic myocarditis, with fibrosis and aneurysmal thinning of the ventricle and no coronary artery disease. Thus chronic myocarditis and chronic constrictive pericarditis must be added to the list just enumerated.

Stress Tests for Coronary Insufficiency

The diagnosis of angina pectoris is not always straightforward. Although in the great majority of patients one can establish or eliminate this diagnosis with a carefully taken clinical history, there are still a few cases with which one must remain in some doubt. Various stress tests, some standardized, others carried out more or less "by ear," have been proposed to help settle these doubts. Opinion is still divided as to their value. Master's group has emphasized that abnormal two-step exercise tests are not specific for coronary artery disease since other organic or functional states, such as rheumatic, luetic, or congenital heart disease or severe anemia, may be the underlying cause. On the other hand, the test may be abnormal in from 6% to 8% of normal people and also in patients with neurocirculatory asthenia or anxiety states. They further claim that, where the test is abnormal, differentiation between a true and a false-positive test may be made on clinical grounds, which makes one wonder whether in such cases the test should be done at all! One lesson from my own experience: never do a Master test in a patient whom you know full well has functional heart disease merely to satisfy him that he has no organic heart disease. He may well turn out to have a positive test.

The varying experience of the Hopkins group [5] would, if confirmed, cast considerable doubt on the validity of the entire Master test approach to the diagnosis of coronary insufficiency. These workers found that the electrocardiographic response to exercise was positive by Master's criteria in 22.8% of normal controls and in 50% of subjects with angina pectoris or old myocardial infarction. The experience at this hospital, not yet tabulated in detail, lies somewhere between these extremes. We have found the test to be quite helpful in certain doubtful cases. The occasion for doing this test is infrequent. We have had a very high yield of equivocal results. In the tracing recorded immediately after exercise, which is generally the most informative, the base line frequently wanders so widely that it is difficult or impossible to determine the true point of reference. Furthermore, the RS-T junction (point "j") may not break sharply but, rather, form a smooth, indeterminate slur. We have not considered the test positive unless the depressed RS-T segment moves horizontally or downward before regaining the isoelectric line. Master [6] has recently recommended the routine use of leads 2, V_3, V_4, and V_5 over the formerly used leads 1, 2, 3, and V_4 in the performance of his test.

The RS-T segment depression which is characteristic of spontaneous or induced coronary insufficiency resembles that seen in subendocardial infarction. By analogy, it is held that it is the subendocardial laminae which are vulnerable to the effects of hypoxia in coronary artery insufficiency. It is important to remember that a similar, if not identical, electrocardiographic picture may be produced by digitalis in therapeutic doses. There is some evidence that digitalis in toxic doses may actually produce myocardial necrosis and that this damage may have a predilection for the subendocardial laminae of the ventricle. There may be an enhancement phenomenon here, too, for it is quite well established that digitalis itself may induce a "false-positive" Master test, in the absence of coronary artery disease. A tracing reproduced by Yu and Soffer [7] shows diagnostic RS-T segment depressions during and after exercise after digoxin administration and no such change without digoxin. A new wrinkle is introduced into the exercise test by the Rochester workers,[8] who have utilized a three-minute treadmill test with a precordial lead. The exercising limbs do not interfere with the recording of the precordial lead, and the latter is generally much more useful than an extremity lead in the detection of coronary insufficiency anyway. With this technique these workers have found, in certain instances, diagnostic changes only in tracings taken during exercise, thus augmenting the sensitivity of an exercise test.

A study by Ramsey and Beeble [9] showed that most patients with mitral stenosis of moderate severity had positive Master tests. Many of these were in patients not receiving digitalis. An example of this is shown in figure 2, made from tracings which these workers were good enough to send me. Note that cupped depressed RS-T segments were present before exercise and that pronounced shifts were recorded after exercise.

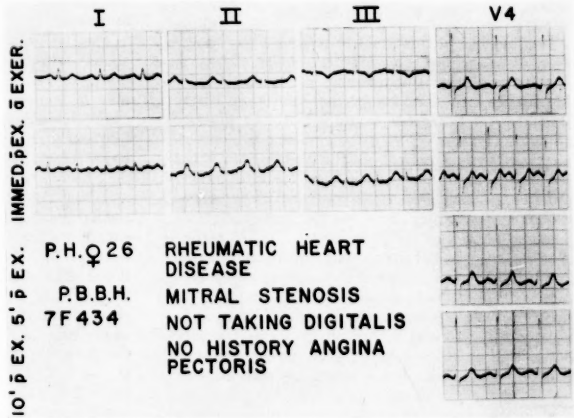

Fig. 2.—"Positive" Master test in absence of coronary artery disease. Patient was 26-year-old woman with rheumatic mitral stenosis, not taking digitalis.

The beat after a long pause may exhibit precisely the same QRS complexes as the beats preceding the pause, but its T wave may differ widely from the antecedent T waves. This would therefore correspond to what Wilson has called a "primary" T-wave change. It was first considered that this phenomenon occurs only after the pause set up by extrasystoles. Accordingly it was given the polysyllabic tongue-twister, "postextrasystolic T-wave changes." However, similar changes have also been observed in the beats after the pauses in sinus pauses, sinoauricular block, second degree auriculoventricular block, conducted or nonconducted auricular premature beats, and auricular fibrillation, as well as in ventricular premature beats. The height and direction of the T wave, of the U wave,

or of both and the duration of the Q-T interval may be affected. As a general thumbnail rule, these changes should not be regarded as significant unless they are striking, compelling, and obvious at first sight. It has been our continued experience at the Brigham hospital [10] that changes of this type are usually correlated with myocardial impairment, generally myocardial ischemia. There is some degree of correlation between this postpausal T-wave change and the so-called positive Master test. In fact, we have come to look on the scrutiny of post-extrasystolic beats as a "built-in Master test." This phenomenon has been explained variously as the direct result of changes in cycle length per se, in the degree of diastolic filling and systolic emptying of the ventricles, in the volume of coronary flow, or in the contact of a distended ventricle with the chest wall.

Serial Electrocardiograms

I would like at this point to make a few derogatory remarks about the widespread habit of recording frequent and unnecessary electrocardiograms in patients with acute myocardial infarction. I have seen the most flagrant examples of this practice among interns in whom it is condoned as a necessary part of their education. But this custom is not confined within hospital walls; it is rife among practicing physicians. At $5, $10, or $15 per set of tracings, this further increases the already difficult financial burden of the patient.

When the clinical diagnosis of acute myocardial infarction is suspect and electrocardiographic support for that diagnosis is yet lacking and no alternative diagnosis has been established, one can have no quarrel with the recording of serial tracings. Sometimes it takes days or even weeks for such changes to appear. But it must be insisted that once a diagnosis of acute infarction has been settled on the basis of dynamic sequential changes there is no good reason for willy-nilly repetition of the electrocardiogram.

The most common reason given for ordering repeated electrocardiograms is to obtain evidence for extension of infarct. Yet it is only under the most unusual circumstances that the electrocardiogram, as such, gives evidence of this development. The electrocardiogram, in fact, is notoriously inaccurate in demonstrating extension. Much more often than not the clinical story of redevelopment of pain, dyspnea, shock, or sweating is much more helpful in making this inference. Many electrocardiographers, from the finding of absent R waves perhaps in leads V_1 and V_2 at the initial examination and absent R waves in leads V_1 through V_4 or V_5 at a subsequent recording, will conclude that the area of anteroseptal myocardial infarction has widened. On the other hand, one of the electrocardiographic clues to pulmonary embolism is a leftward migration of the so-called transitional zone. The latter is the precordial point or area to the right of which one type of potential, e. g., RS, and to the left of which another type of potential, e. g., QR, is recorded. Such a twist of the heart might be assumed if this transitional zone moved during a clinical episode from, for instance, position V_2 or V_3 to or beyond V_6. Moreover, RS-T segment elevations and T-wave inversions may develop over the right precordium in acute cor pulmonale, as well as in acute anteroseptal infarction. Furthermore, a shift of the transitional zone may occur in acute myocardial infarction when neither lateral extension nor acute cor pulmonale is demonstrable, presumably as the result of a slight change in the position of the heart or in the position of application of the precordial electrodes. If evidence for acute anteroseptal infarct has already been at hand, how can one say whether the change described signals extension of infarct, acute cor pulmonale, or nothing? Clearly the decision is not as easy as may at first sight appear.

Another example of this difficulty: Patients with acute posteroinferior myocardial infarction with QRS, RS-T, and T-wave changes detected initially only in leads 2, 3, and aVF, who later show the same changes also in lead V_6 or V_5 and V_6, are frequently regarded as having extended their posterior infarct laterally. Often this change occurs in the absence of clinical evidence of fresh infarction and in a day or two the changes in the left precordial leads disappear, never to reappear. One cannot escape the conclusion that these changes were present over the left precordium as a positional phenomenon, the infarctional changes rotating into and out of relation with the left lateral precordium. It would be an exaggeration, however, to say that the electrocardiogram is of no value in the detection of spread of the area of infarction.[11] If, for example, the RS-T segment elevation in leads 2, 3, and aVF has returned to or toward the isoelectric line and there now develops RS-T segment elevation and deep inversion of the T waves, as well as prominent Q or QS waves over the left precordium, the inference of lateral extension of a posterior infarct might be justified. In such a case, however, one would expect concurrent clinical changes.

Ordinarily in acute myocardial infarction one observes a characteristic progression of the RS-T and T-wave changes. At first the RS-T segment may be elevated and the T wave still upright. Then, as the degree of RS-T segment elevation becomes less pronounced, the T wave shows terminal inversion. As the RS-T segment reaches the isoelectric line, the T wave may show deeper and deeper inversion. There are many variations on this theme. One that has interested me is the occasional temporary interruption and retrogression rather than continued progression in this type of sequence. Figures 3 and 4 were each recorded in classic, uncomplicated attacks of acute myocardial infarction. In figure 3 the late inversion of the T wave, which seems to be headed to a deeper

inversion, is halted temporarily, but the sequence of deeper and deeper inversion is resumed in subsequent tracings. A similar phenomenon is observed in figure 4, where the usual sequence is transiently interrupted.

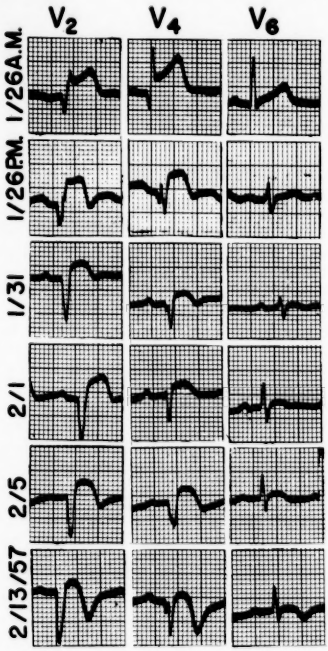

Fig. 3.—Interrupted sequence of electrocardiographic changes in acute anteroseptal infarction. Tracing of 2/1/57 shows retrogression toward earlier type of change without coincident exacerbation of symptoms; in subsequent tracings characteristic sequence is resumed.

When a series of this kind was first observed, the tendency was to attribute it to an error in the chronologic dating of the electrocardiograms, but with further experience it became clear that this was a real change. An authority on the subject of electrocardiography suggested that this phenomenon might be related to complicating pericarditis or perhaps to extension of the infarct. I have since studied the clinical charts of some 30 individuals showing such changes and could find nothing in their behavior or in the correlative laboratory data to confirm either of these possibilities. So many hearts with acute infarction show fibrin deposits on the epicardial surface anyway, and extension is such a difficult thing to establish in the face of such a continuum of pathological processes, as characterizes uncomplicated myocardial infarction, that either of these possibilities is generally extremely difficult to establish and, in the last analysis, is probably little more than a guess. It seems that this interrupted sequence is a benign electrocardiographic curiosity with little if any clinical or pathological counterpart. It was suspected that this change may be the result of electrolyte shifts, but chemical observations were too infrequent in these cases to establish this possibility. The phenomenon is perhaps a byproduct of the observation of frequent unnecessary electrocardiograms.

Persistent RS-T Segment Displacements

Ordinarily, the RS-T segment shifts that occur in acute myocardial infarction are transitory. The RS-T segment returns to the isoelectric line within a week or two. In some instances, however, these shifts persist for a longer time or even indefinitely. A case was reported by Rosenbaum, Johnston, and Alzamora[12] in which displacements of this type were present for more than two months. The patient had mediastinal neoplasm. Postmortem examination showed no coronary artery disease or

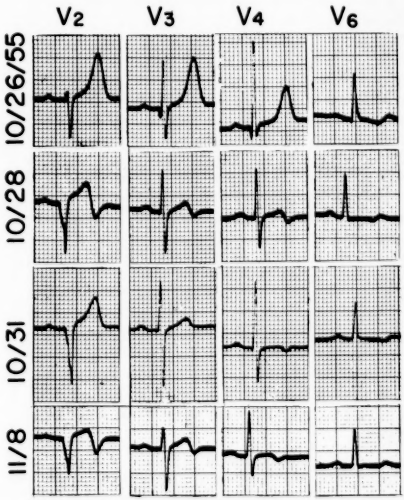

Fig. 4.—Transient electrocardiographic retrogression (similar to that in fig. 3) in acute anteroseptal infarction associated with leukocytosis and elevation of sedimentation rate. No new symptoms developed at time of interruption of sequence; final tracings show resumption of classic type of changes.

myocardial infarction. It did show that the heart was invaded by neoplasm. Changes of this type have been observed much more frequently with aneurysm of the ventricle. In fact, persistent RS-T segment shift should be considered an important clue to that condition. The important practical point is that this finding is often misinterpreted as

indicating an acute myocardial infarction and, in fact, is frequently the cause for repeated hospitalizations. In the absence of other laboratory or clinical data substantiating that possibility and when it is appreciated that this is a fixed rather than dynamic change the diagnosis of fresh infarction is no longer tenable.

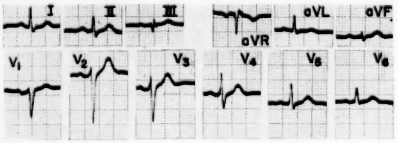

Fig. 5.—Normal electrocardiogram in patient said to have had heart attack one year previously.

Katz has considered this phenomenon a manifestation of chronic coronary insufficiency. The thesis is that, perhaps as a result of ischemic changes in the myocardium bordering on the aneurysm, electrical changes are developed repetitively with each beat. Alternatively, the changes could be explained, in part at least, by the chronic pericarditis which occurs in the overlying epicardium in many of these cases or, perhaps, by the repetitive contact of the epicardium with the chest wall producing with each beat a "current of injury." But the explanation which thus far seems best to satisfy the facts is that offered by Myers. He suggests that the changes are to be viewed as a reflection of the cavity potential inscribed at the endocardial aspect of the ventricular wall opposite the aneurysm. Since this ventricular wall is invariably hypertrophied and since the potential at the endocardial aspect of the hypertrophied ventricle is a reciprocal of the potential at its epicardial aspect, one would expect to find elevation of the RS-T segment in the cavity. The electrode "looking through the aneurysmal window" sees these changes unaltered. It must be confessed, however, that the analogy of the electrical window has been roundly criticized and that, as yet, no simple explanation is forthcoming which can explain all the electrocardiographic findings.

T Wave Changes Only

Ordinarily, changes in the QRS complex are a prerequisite to the diagnosis of myocardial infarction. There are some cases of acute infarction, however, in which changes develop only in the T waves. If these changes occur during a classic acute clinical episode and in association with other laboratory evidence of tissue breakdown, a clinical diagnosis of acute infarction is justified. The opinion that the prognosis is favorable in individuals showing such changes has recently been questioned by Cutts and co-workers.[13] If T-wave changes persist over two or three days, one must, on a priori grounds alone, suspect the possibility of actual myocardial necrosis even if there is no correlative clinical or laboratory evidence for infarction. The hypothesis would be that myocardial ischemia, long continued, must inevitably lead to necrosis. At autopsy, such hearts may show either intramural infarction or multiple punctate subendocardial necroses. Apparently the latter do not present over a large enough front to produce RS-T segment shifts. At times, T-wave inversion may be limited to the mid-precordial leads. Such a change noted during a suspect clinical episode may represent the premonitory stage of acute transmural infarction and is thus an indication for recording serial electrocardiograms.[14]

The Vanishing Infarct

Let us suppose that a patient tells you that he was treated a year ago at another city by another physician and that he was told that he had had a heart attack. Suppose also that you now find him quite unremarkable on physical examination and that the electrocardiograms which you record look like those in figure 5—a normal electrocardiogram. You might well harbor the suspicion that the previous examining physician was either a rascal or a fool. If you now contact this physician he might well send you a series of tracings recorded 15 months previously, which are classic for acute anteroseptal infarction (fig. 6). In point of fact, each set of tracings was recorded in the same patient on separate admissions at the Peter Bent Brigham Hospital on the dates indicated. The patient's story and his physician's diagnosis were, therefore, well founded.

Changes in the QRS complex are generally the most difficult to produce and the most difficult to lose, but occasionally a pathological Q wave which develops during an acute myocardial infarct will disappear after a day or two, perhaps never to reappear. The cause of this phenomenon has never been established. It has been attributed to a "knocking out" but not actual death of myocardium. Such an explanation hardly seems applicable in the present case. Changes of this type, but less pronounced in degree, have been attributed to the contraction and virtual disappearance of the myocardial scar, but it is most unusual to observe the disappearance of such widespread and convincing evidence of infarction as this. Sometimes R waves

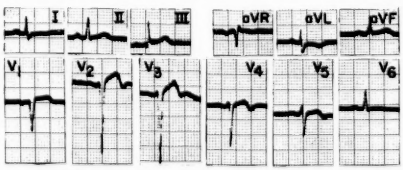

Fig. 6.—Tracings of same patient as in figure 5, recorded 15 months previously. (This was not isolated appearance but last of series of tracings showing classic evolution of acute anteroseptal myocardial infarction.)

will reappear over the right precordium in a patient with anteroseptal infarct on the supervention of a fresh posterolateral infarct. The forces activating the left posterolateral aspect of the heart are no longer present and therefore fail to antagonize the opposing forces activating the right anterolateral aspect of the heart. The latter are then able to express themselves unopposed. The fact that in the present case evidence for posterior infarction is not at hand by no means dismisses that possibility. Whatever the mechanism, the moral is clear. The experience of the vanishing infarct is not extremely rare. Whenever a patient states that he has been treated for coronary thrombosis and the electrocardiogram seems at variance with that diagnosis, an effort should always be made to study the tracings recorded at the time of the acute episode before discarding the diagnosis.

The Infarct as a Chemical Phenomenon

One of the major struts of the science of electrocardiography has been electrocardiographic-pathological correlation. For years electrocardiographers have sought vindication in the anatomic verification of their deductions from the electrocardiogram. Various explanations have been offered when such substantiation was lacking. Where, for example, myocardial infarction was diagnosed but no such anatomic lesion demonstrated, it has been at times averred that the lesion was still in its biochemical phase; the anatomic phase simply has not yet been attained. In the past, such claims have been made loosely and on a priori grounds. But support for this attitude has recently been offered by the results of the technique of histochemistry. A decrease of certain enzymes may be detected when routine staining techniques show no obvious changes. The studies of Wachstein and Meisel[15] of succinic dehydrogenase activity in clinical and experimental myocardial necrosis showed a reduction of enzymatic activity as early as two hours after the onset of symptoms and extension to fibers which showed no significant changes with routine staining techniques.

The electrocardiographic changes of acute pericarditis are generally considered to depend on changes in the subepicardial myocardium. Recent experiences in the treatment of potassium intoxication with the artificial kidney[16] raise the question of whether these changes actually result from changes in electrolyte balance, whether or not they are subsequently demonstrated to be associated with an anatomic lesion. It seems reasonable that a change which can be eliminated by dialysis should be considered a chemical change. Would this same reasoning apply to a dialyzable "current of injury"? A number of patients with acute potassium intoxication showed electrocardiographic changes closely resembling or identical with the tracings of acute myocardial infarction or pericarditis.

Before he was subjected to hemodialysis, a 40-year-old man with acute carbon tetrachloride poisoning showed changes which worried the attending staff as to the possible existence of acute anteroseptal infarct (fig. 7). This change almost completely disappeared with use of the artificial kidney but returned on the following day. He died later that day of acute pulmonary embolism. The pathologist estimated that embolism had been going on for three days or more. It is not certain that the RS-T segment shift was the electrocardiographic manifestation of acute cor pulmonale, but its elimination by dialysis was of considerable interest.

A 21-year-old man sustained severe vertebral and abdominal injuries in an automobile accident. He developed a massive intraperitoneal hemorrhage and was transfused with incompatible blood. He thereupon developed renal shutdown and potassium intoxication. On numerous occasions, in addition to the characteristic evidence of potassium intoxication, his tracings showed elevation of the RS-T segments in leads V_1 and V_2 which receded with use of the artificial kidney. This phenomenon repeated itself several times during his clinical course. He eventually recovered. (Two other patients showed similar amelioration of these shifts; at postmortem examination one of these was seen to have had definite uremic fibrinous pericarditis.)

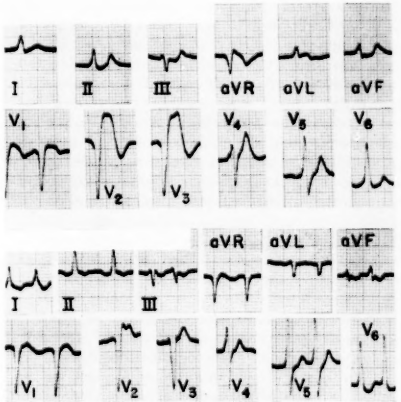

Fig. 7.—"Dialyzable current of injury": tracings recorded in 40-year-old man with acute renal shutdown. Tracings recorded before those illustrated showed classic changes of potassium intoxication and left bundle-branch block. *Above*, those recorded before use of artificial kidney show deep, broad Q waves and elevated RS-T segments over right precordium, characteristic of acute anteroseptal infarction. *Below*, after dialysis, QRS complex sharpened and shortened and RS-T elevation almost disappeared. Postmortem examination showed acute pulmonary embolism, no coronary artery disease or myocardial infarction.

When discussing the chemical aspects of myocardial infarction, one cannot help but mention the resemblance between the T waves of potassium intoxication and those of posterior myocardial infarction. In contrast to other causes of T-wave peaking, the T waves of potassium intoxication tend to be narrower, to show a greater tendency to be tall and narrow and steep and pointed, and to be associated with terminal slurring of the QRS complex.[17] However, this morphologic differentia-

tion is difficult. Ordinarily, the clinical differentiation is not difficult because of the different setting in which each occurs, but we have now seen two or three cases in which myocardial infarction has been complicated by severe hypotension, acute renal failure, and potassium intoxication. In each of these cases potassium intoxication was the immediate cause of the fatality.

The Role of the Electrocardiographer

There are various shades of gray between black and white. Certain electrocardiographic appearances may be diagnostic of, some may be characteristic of, some suggestive of, and some merely compatible with a certain condition. Sometimes the electrocardiogram may suggest not one but a number of possibilities. It is imperative that the electrocardiographer in all honesty should list those possibilities. In doing so, he will place them in what he considers the order of their probability.

In reading x-ray films, our roentgenologist emeritus, Dr. Merrill Sosman, was in the habit of giving two readings: first, a cold reading, unbiased by the requisition form and based on examination of the films alone; second, a rereading of the films after hearing the clinical story. A similar approach has been of inestimable value in the reading of electrocardiograms. Then the clinician, whether another person altogether or the electrocardiographer functioning now as a clinician, should evaluate the electrocardiographic interpretation in relation to the clinical picture. He may find any or all of the listed possibilities to be absurd, unlikely, or impossible or he may find that they give added support to his clinical impression. It is then his duty to accept or reject them. An understanding of and sympathy with these limitations of electrocardiography is urged on the self-styled "practical" clinician or surgeon. The electrocardiographer, on the other hand, should not allow himself to be stampeded into an unequivocal statement when only an equivocal interpretation is warranted.

Summary and Conclusions

In patients with coronary artery disease it is worthwhile to note whether the electrocardiographic appearance is fixed or changing. The changes may be rapid in development, as in spontaneous or induced coronary insufficiency, slower in development, as in acute myocardial infarction, or fixed, as in ventricular aneurysm. In some cases of myocardial infarction the electrocardiogram may show changes in the T waves only; in the presence of a clearcut story and evidence of tissue breakdown, the diagnosis of infarction may be justified. The RS-T segment changes characteristic of subendocardial ischemia, if persistent over days and associated with a convincing clinical episode and correlative laboratory evidence, suggests actual subendocardial infarction. Although the electrocardiogram can furnish evidence for extension of a myocardial infarct, there is no warrant for indiscriminate repetition of the electrocardiogram once the diagnosis of acute infarction has been established. In the absence of a clinical counterpart those changes which may be observed are of dubious significance. Classic electrocardiographic signs of old myocardial infarction may be recorded in chronic constrictive pericarditis or chronic myocarditis. This results from the inability of the electrocardiogram to distinguish between fibrosis due to vascular disease and that due to other causes. In rare instances all electrocardiographic evidence of well-documented myocardial infarction may disappear.

Experience with the electrocardiogram in constrictive pericarditis and in subendocardial infarction leads some support to Prinzmetal's concept of activation of the ventricular wall.

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TRIAMCINOLONE IN TREATMENT OF RHEUMATOID ARTHRITIS

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The addition of a fluorine atom at position 9α to hydrocortisone, so-called halogenation, increases the anti-inflammatory effect over that of hydrocortisone 7 times, the antirheumatic effect 10 times, and the glycogen-depositing effect 13 times, but also increases the sodium-retaining effect to at least 50 times that of hydrocortisone. The addition of a double bond between carbon atoms 1 and 2 to form Δ 9α-fluorohydrocortisone results in about equal anti-inflammatory and antirheumatic effects but no lessening of the sodium-retaining properties. However, the addition of a hydroxy radical at position 16 to this latter compound, while decreasing considerably the antirheumatic effect (now four times that of hydrocortisone), completely neutralizes the salt-and-water-retaining properties, producing in fact what appears to be a sodium-excreting effect. Corticosteroid therapy in the management of rheumatoid arthritis should be undertaken only after serious consideration of the potentialities of the steroid used and the side-effects and other risks involved. It is most important to stress the fact that the degree of intensity of any side-effects that will lead a physician to discontinue the use of a drug, particularly a corticosteroid, is variable. Triamcinolone was found to be supressive of inflammation and rheumatic manifestations in doses roughly proportional to those of prednisone and prednisolone. The advantages of triamcinolone over previously used corticosteroids appeared to be fewer and less severe gastrointestinal symptoms, less psychic irritation, and no effect on arterial blood pressure. It was found, however, to retain many of the troublesome side-effects of the other corticosteroids.

I report here my experience with the effect of a new synthetic corticosteroid designated as 9α-fluoro-16α-hydroxy-Δ¹-hydrocortisone and its diacetate ester, triamcinolone (Aristocort). I have used it in the management of rheumatoid arthritis, osteoarthritis, and some other allied rheumatic disorders, but only my observations in the treatment of rheumatoid arthritis will be presented here.

Corticosteroid therapy in the management of rheumatoid arthritis should be undertaken only after serious consideration of the potentialities of the steroid used and the side-effects and other risks involved. It is my opinion that it should be considered in only four situations: (1) when rheumatoid arthritis is fulminating and does not promptly respond to adequate salicylate therapy; (2) when the physician is unable to maintain the patient in reasonable comfort with rest, corrective exercises, salicylates, and constitutional therapy; (3) when gold salts fail after an adequate trial; and (4) as a temporary measure just before, during, and after some orthopedic and rehabilitative procedures.

The corticosteroids are administered with too little consideration of their potentialities, particularly their untoward effects. In mild rheumatoid disorders the side-effects may well be more disturbing than the disease itself. Added to the invariable development of at least some side-effects are the possibilities of more or less dependence on the steroid, making it almost impossible to stop therapy with the drug. Also, there is the possibility of serious debilitating withdrawal symptoms and at times a periarteritis nodosa–like syndrome when therapy with the drug is finally stopped.

However, there is little doubt that the physician at times has patients with rheumatic conditions, particularly chronic rheumatoid arthritis, that may be intractable to other forms of therapy. Here a corticosteroid with minimal side-effects is the ideal sought, short of a specific cure of the basic disease itself. Since 1949, efforts have been con-

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tinuing to develop a corticosteroid with maximum anti-inflammatory and antirheumatic effects but minimum unwanted side-effects.

Chemical Structure

The addition of a fluorine atom at position 9α to hydrocortisone, so-called halogenation,[1] increases the anti-inflammatory effect over that of hydrocortisone 7 times,[2] the antirheumatic effect 10 times,[3] and the glycogen-depositing effect 13 times,[4] but also increases the sodium-retaining effect to at least 50 times that of hydrocortisone.[5] The addition of a double bond between carbon atoms 1 and 2 to form Δ^1 9α-fluorohydrocortisone results in about equal anti-inflammatory and antirheumatic effects but no lessening of the sodium-retaining properties. However, the addition of a hydroxy radical at position 16 to this latter compound,[6] while decreasing considerably the antirheumatic effect (now four times that of hydrocortisone), completely neutralizes the salt-and-water-retaining properties, producing in fact what appears to be a sodium-excreting effect. This new compound, triamcinolone (9α-fluoro-16α-hydroxy-Δ^1-hydrocortisone) is the one reported in this study. Sodium excretion is evident in man during the first three days of balance studies,[7] and potassium remains essentially in equilibrium. Balance studies in humans show slight but questionable loss of nitrogen, calcium, and phosphorous.[8]

Clinical Material

Since December, 1956, I have treated 105 patients with triamcinolone, all suffering from one of the following forms of arthritis or allied rheumatic disorders: rheumatoid arthritis (67), rheumatoid spondylitis (5), osteoarthritis (21), and miscellaneous rheumatic disorders (12).

At first we used the diacetate form of triamcinolone but later the free alcohol. The clinical differences appeared to be minimal and negligible. Two-milligram tablets were used, the daily dose always being given in four divided amounts, usually after meals. No dietary restrictions were advised, the subjects being allowed to use salt as they pleased. No supplemental potassium was given.

In this report only the effects of triamcinolone on rheumatoid arthritis will be dealt with in detail. The effect on osteoarthritis is a separate and distinctly different consideration in that here we are dealing with a structural degeneration, the degeneration of cartilage, the symptoms of pain probably being due to the sequential change in anatomic structure. Pain in osteoarthritis is the result of undue stress that eventually causes an inflammatory reaction of the soft tissue structures supporting the joints involved. Most observers feel that the symptoms of osteoarthritis can be handled much more effectively and with a minimum of risk by basic medical and orthopedic correction of the traumatic stresses. The corticosteroids are not needed except at times at the beginning of treatment to allay the acute discomforts of the superimposed traumatic arthritis and in patients with well-advanced osteoarthritis, where structural changes are great and the effects of these changes extremely painful and debilitating and not susceptible to medical or surgical orthopedic measures.

The subjects with rheumatoid arthritis totaled 67. Twenty-three of these were treated for at least 6 months and up to 11 months. Of the total of 67 patients with rheumatoid arthritis, 44 are still under treatment with triamcinolone, while therapy with the drug was stopped in 23 patients before six months for the following causes, some patients showing two or more of those mentioned: weakness and fatigue (6), tachycardia (5), leg cramps (5), minor gastrointestinal complaints (5), recurrence of old duodenal ulcer symptoms (1), emotional unrest (4), headache (3), hirsutism (3), persistent respiratory infection (1), glucose tolerance decrease (1), excessive weight gain (1), no improvement (1), and unrelated death (1).

It is most important to stress the fact that the degree of the intensity of any side-effects that will lead a physician to discontinue the use of a drug, particularly a corticosteroid, is variable, some ignoring any but the most marked side-effects, even going to the extent of trying to counteract the side-effects by therapy, such as insulin for patients with increased diabetes or alkalizers for patients with peptic ulcer symptoms, rather than decreasing the dose or eliminating the drug. It is my opinion that this is a dangerous procedure. In such conditions as disseminated lupus erythematosus, where the corticosteroids are lifesaving, there is justification for such a policy. I do not think it is justified in rheumatoid arthritis. In this study I have discontinued the use of corticosteroids when the side-effects were even slightly greater than minimal. This difference in attitude as to the relative importance of side-effects from corticosteroids is widespread and makes it almost impossible to compare the published incidence and degree of side-effects resulting from the various compounds so far studied.

Long-term Administration

Twenty-three of the 67 patients have received the drug for over 6 months and up to 11 months. All 23 had unquestioned rheumatoid arthritis, the average duration of the disease being over 15 years. They were well advanced in their disease, mostly in stage and class 3 and 4. Nineteen of the 23 had been on therapy with prednisone or prednisolone before starting therapy with triamcinolone, all but one for over a year, and all of these patients had experienced one or more side-effects, usually severe enough to make it desirable or obligatory that steroid therapy be changed or stopped.

The therapeutic results were good, 16 of the 23 showing a grade 2 and 6 a grade 3 response. In one patient, therapy with the drug had to be stopped after six months because of a lack of satisfactory therapeutic response from doses greater than average, even though he showed no important side-effects. How many of the good results will be maintained after 6 to 11 months is a question only the future course can answer. With previously used corticosteroids it was fairly common for initial good results to decrease or disappear even after months of satisfactory suppressive action.

The average dose of triamcinolone necessary to maintain adequate antirheumatic effect was 10 mg. a day in four divided doses, comparable to the usually stated maintenance dose of prednisone and prednisolone. Thus in our experience the suppressive effects of triamcinolone and prednisone are about equal. As a rule, therapy was started with a dose larger than this, the initial dose commonly being around 24 mg. a day.

Undesirable Side-effects

Of the total 67 patients with rheumatoid arthritis, all without exception showed unwanted side-effects of some kind. Most of these, however, were minor. The side-effects in the 23 patients who underwent long-term therapy, particularly as compared to the side-effects during previous prednisone or prednisolone therapy, can be summarized as follows: The most notable observations were that edema and high blood pressure were not observed and, when they had been present with use of prednisone and prednisolone (in 4 of 19 and 5 of 19 patients respectively), uniformly disappeared. Euphoria and psychic unrest, usual sequelae previously, were very uncommon. In five patients who, while receiving prednisone or prednisolone, were having exceedingly severe duodenal ulcer symptoms, one with bleeding, a shift to triamcinolone resulted in almost immediate cessation of peptic ulcer symptoms. Such gastrointestinal complaints as flatulence, nausea, and epigastric discomfort were noted in some, but in only one patient in 67 could these be called a peptic ulcer syndrome, and in this patient it was a recurrence of a previously proved ulcer. However, x-rays were not done routinely. The incidence of so-called silent ulcers and the question whether these patients will develop a peptic ulcer in the future, only time and x-rays can decide. No ulcer diets, antacids, or anticholinergic drugs were used in any case. The over-all impression was that gastric symptoms, while frequently present, were far less common and less severe than those with previously administered corticosteroids.

Such unwanted effects as facial rounding, hirsutism, and cutaneous purpura were noted about equally with prednisone, prednisolone, and triamcinolone. While most patients who are on therapy with other corticosteroids gain weight, most of the patients taking triamcinolone lost weight, probably due to water loss and not to protein loss and muscle wasting, as the weight loss was usually confined to the first few weeks of the medication only. In view of the reported excessive weight loss observed by some investigators after administration of triamcinolone, I was careful to note this point. In no case was the weight loss as much as 10% of the original weight. Some of the excessive weight loss observed by others may have been in cases where the patient had been receiving other hormones and had excessive initial water retention. Also the well-recognized appetite-curbing effect of triamcinolone is undoubtedly a factor. No new diabetes developed, and in the over-all series the condition of patients who already had diabetes was not adversely affected.

One side-effect that appeared to be more frequent with triamcinolone than with other corticosteroids was leg and foot cramps, especially at night, often requiring the patient to get up and walk about. The over-all incidence in the 105 cases was about 16%. These leg cramps could not be correlated with such abnormal findings as changes in the oscillometric readings or in calcium, sodium, potassium, and other blood studies. At times, these cramps were severe enough to induce me or the patient to discontinue therapy with the drug, but if the administration was continued this particular side-effect often disappeared.

Further experience with triamcinolone over a longer time than 6 to 11 months will undoubtedly reveal other untoward effects. No observations were possible as to the presence or absence of osteoporosis sequential to the use of this drug. To date, however, this corticosteroid stands out as advantageous in four important respects: 1. There is a uniform absence of edema, probably due to its lack of salt-retaining properties. 2. Gastric irritation and peptic ulcer symptoms are less frequent. 3. There is lessened psychic irritation. 4. There is a lack of effect on the arterial blood pressure. These are the four side-effects that plagued patients most severely with previously used corticosteroids. In other respects the incidence of side-effects is similar, although their development seems to take longer on average anti-inflammatory doses. To date triamcinolone is the safest effective corticosteroid I have used.

Summary

A new synthetic steroid, 9α-fluoro-16α-hydroxy-Δ^1-hydrocortisone, and its diacetate, triamcinolone (Aristocort), used in the treatment of rheumatoid arthritis, appears to have four important advantages over other steroids in almost all cases: (1) lack of the production of edema; (2) less gastrointestinal symptoms, particularly the peptic ulcer syndrome; (3) less psychic irritation; and (4) no effect on arterial blood pressure.

Triamcinolone was found to be suppressive of inflammation and rheumatic manifestations in doses roughly proportional to those of prednisone and prednisolone. This effect was established more slowly with triamcinolone than with the other corticosteroids, but at the same time unwanted side-effects were slower in asserting themselves. Triamcinolone, however, was found to retain many of the disturbing side-effects of the other corticosteroids, particularly its masculinizing effects, facial rounding, cutaneous purpura or ecchymosis, and acne. Increased sweating and leg cramps were prominent.

580 Park Ave. (21).

The triamcinolone used in this study was supplied as Aristocort by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

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CLINICAL NOTES

CARDIAC ACTIVITY IN AN APNEIC FIVE HUNDRED EIGHTY GRAM HUMAN FETUS

MAINTAINED FOR TWENTY-ONE HOURS AT TEMPERATURES BETWEEN 22 C AND 0.1 C

James A. Miller Jr., Ph.D.
and
Antonio Marini, M.D., Stockholm

Nine years ago, the rationale for the use of hypothermia in asphyxial conditions was discussed and preliminary data were presented which showed that cooled animals tolerate longer exposures to asphyxia than do animals at normal body temperatures.[1] Subsequently, these results were confirmed and extended by experiments on several hundred neonatal and adult guinea pigs.[2] Even more striking benefits in asphyxia have been reported for hypothermia in the case of neonatal rabbits and puppies, which are less mature at birth than the guinea pig.[2b] In all species investigated, the newborn member is more tolerant of hypothermia than the adult of the same species. In addition, tolerance is greater in those species which are less mature at birth than in those which are more mature. Accordingly, it has been suggested that, in all probability, the full-term human infant can tolerate lower temperatures than the adult and that the premature infant is still more resistant to cold.[2]

Recently an opportunity was presented for studying the effects of hypothermia on the cardiac activity of a 580 Gm. (1.25 lb.) female fetus on which a craniotomy had been performed during a legal abortion. As may be seen from the account which follows, the heart of the premature fetus not only can tolerate cardiac standstill of one hour's duration at 0.1 C but, even when its oxygen supply is severely limited, actually recuperates during such periods of inactivity.

From the Wenner-Gren Cardiovascular Research Laboratory. Dr. Miller is a Senior Postdoctoral Fellow, National Science Foundation, from the Department of Anatomy, Emory University School of Medicine, Emory University, Ga. Dr. Marini is a Swedish Government Fellow from the Department of Pediatrics, University of Ferrara, Italy.

Procedure

The baby was placed in isotonic glucose solution at 2 C immediately after delivery. It arrived at the laboratory, 35 minutes later, with a body temperature of 25 C and was totally immersed in fresh

glucose solution at 2 C. Heparinized type O blood, saturated with 95% oxygen plus 5% carbon dioxide, was delivered to the fetus at intervals through a catheter inserted into the umbilical vein. Since only a small amount of this type of blood was available and difficulties with perfusion were encountered, only 300 ml. of the blood was used during the entire period of observation. No attempts were made either to close the craniotomy incision or to staunch the flow of blood which seeped from the wound. The chief function of the perfusion blood was to replace that lost. However, at higher temperatures deterioration of the electrocardiogram (ECG) was noted when perfusion was stopped for any length of time. Since the incision was over the area of the respiratory centers, no attempts were made to induce respiratory movements.

A thermistor was inserted 4 cm. into the colon. Electrocardiographic leads from a two-channel direct-writing electrocardiograph were attached to the appendages. Throughout the entire study, the gain was kept constant at 20 mm. per millivolt and the rate of movement of the paper at 25 mm. per second. Generally, the electrocardiographic records were made at temperature intervals of 1 C during each of the five periods of cooling and rewarming.

Reduction of body temperature during the first three periods of cooling was produced by placing the basin of isotonic glucose solution containing the fetus in a larger container of melting ice. The lower temperatures during the fourth and fifth cooling periods were achieved by packing the fetus in snow after the temperature of 4 C was reached.

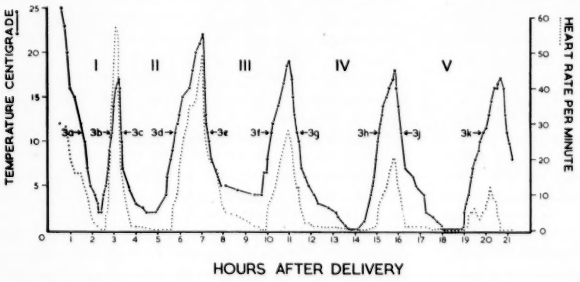

Fig. 1—Temperature and heart rate of 580-Gm. fetus during period of observation.

Observations

Temperature.—On figure 1 is graphed temperature and heart rate during the entire period of observation. From this it is seen that the temperature of the fetus reached 2 C the first and second time it was cooled. The first time it was kept at this temperature for one minute and the second time for 41 minutes. The lowest temperature during the third cooling period was 4 C. During the last two cooling periods temperatures of 0.1 C were achieved. In the fifth period the fetus was kept at this temperature for an hour before rewarming was begun.

In table 1 is a comparison of the lengths of exposure to deep hypothermia during the five cooling periods. On this is recorded the fact that the temperature of the fetus was below 15 C for over 17 hours (1,037 minutes), below 10 C for over 13½ hours (817 minutes), below 5 C for 9½ hours (576 minutes), below 2 C for 4 hours (244 minutes), and below 1 C for almost 2½ hours (148 minutes). The shortest single exposures were in the first cooling period; the longest were in the fourth or fifth periods. If deep hypothermia is a "stressful condition," the last cooling period, with 109 minutes below 2 C and 83 minutes below 1 C, should have produced the greatest challenge to the heart. Actually, as will be seen from sample electrocardiograms, heart action was visibly improved by each period of deep hypothermia.

TABLE 1.—*Length of Exposure to Deep Hypothermia*

Temperature	Cooling Periods, Minutes 1st	2nd	3rd	4th	5th	Total Minutes
Below 15 C	114	117	224	261	261	1,037
Below 10 C	72	143	173	216	213	817
Below 5 C	34	106	108	174	154	576
Below 2 C	1	41	0	93	109	244
Below 1 C	0	0	0	65	83	148

The first rewarming period was arbitrarily terminated at 17 C body temperature. The length of the subsequent rewarming periods was determined by the appearance of the electrocardiogram, and it will be noted that the maximum temperature which the heart could tolerate fell with increasing time. The final stoppage of the heart is attributed to the failure to start the sixth cooling period at 15 C before irreversible changes had developed.

Heart Rate.—Since at very low temperatures there is heart block with complete dissociation of atrial and ventricular beats, the rates of the QRS complexes were plotted as "heart rate" on the graph (fig. 1, dotted line). In addition, there were irregularities in rate and conduction which will be considered later. The most remarkable aspect of observations on heart rate is that contractions were registered at temperatures down to and including 0.1 C. Although at this temperature contractions did not continue indefinitely, several beats were recorded. These were separated by intervals of as long as eight minutes before com-

plete standstill occurred. The method for detecting such widely spaced contractions was not developed until the fourth cooling period. In the last two cooling periods, as the rate approached two beats per minute, the gradually increasing intervals between contractions were timed on a stop watch. This permitted predictions of the time of appearance of future contractions and also the recognition of ECG records in which all phases were so slowed as to be of questionable significance when seen out of context. At the lowest temperatures, QRS intervals of greater than five seconds and maximal deflections of only 0.2 mv. were encountered.

On the graph (fig. 1), it can be seen that, in general, the rate of contraction at a given temperature decreased with time. A further analysis of heart rates is made possible by comparing the rates during cooling and rewarming at temperatures of 16 C, 14 C, 12 C, 11 C, and 10 C (table 2). This shows that after the first cooling period there was an increase in rate which, up through 14 C, was more than twofold. The maximum rate during this first rewarming (and, indeed, during the entire period of observation) was 56 beats per minute at 15 C. By 16 C the rate had started to fall, and at 17 C the second period of cooling was started. Perfusion difficulties encountered during the second cooling period were reflected in the sudden drop in rate to 29 beats per minute at 16 C. Although during subsequent rewarming periods the electrocardiograms showed a great measure of recovery, the rate did not again reach as satisfactory figures as were recorded during the first rewarming period, except at very low temperatures. It may be noted that in the third, fourth, and fifth periods (but not in the second) the rates were greater at each temperature during cooling than they had been a short time earlier during rewarming (compare columns 4 and 5, 6 and 7, and 8 and 9). No suggestions are offered as to the significance of this phenomenon.

Electrocardiogram.—Because the exposures to hypothermia were superimposed on varying degrees of hypoxia, hypercapnia, depletion of energy stores, and increase in concentration of waste metabolites, there are inherent difficulties in interpreting the many changes observed in the ECG. A more detailed analysis of the electrocardiographic record will be presented elsewhere. However, a few samples are shown here in order to illustrate in general the influence of deep hypothermia on cardiac activity. In figure 2 is a comparison of the electrocardiographic records taken immediately after the arrival of the fetus at the laboratory and 66 minutes later after partial rewarming from 2 C. Figure 2*a*, *b*, *c*, *d*, *e*, and *f* are records from six different leads at the start of the first cooling period with the fetus at 25 C. Figure 2*g* and *h* are records of leads 1 and aVL which were taken during the first rewarming period with the fetus at 11 C. These two are directly comparable to figure 2*a* and *e*, since the gain was kept at 1 mv.=20 mm. and the movement of the paper was maintained at the rate of 25 mm. per second throughout the entire period of observation.

An increase in the time required for each stage of the cardiac cycle is to be seen between the records at 25 C and 11 C. However, the most significant difference between the records is in the amplitude of the R wave. The potential change recorded in lead 1 was 0.12 mv. at 25 C, whereas at 11 C it was 1 mv., an eightfold increase. An increase of the same order of magnitude is seen in the records from the aVL lead also (fig. 2*e* and *h*). Decreases in amplitude, as well as slowing of the rate, have been observed in premature infants with more than optimal temperatures and with cyanosis. At lower temperatures, with an improvement in general condition, both the amplitude and the rate increase.[3] For this and other reasons, the amplitude is considered to be a good index of general condition of the heart.

In figure 3 are illustrated sample electrocardiographic records at 11 C which were made before and after each of the five periods of maximal cooling. In the upper row (fig. 3*a*, *c*, *e*, *g*, and *j*) are records taken during cooling after the fetus had been at higher temperatures. The records in the lower row (fig. 3*b*, *d*, *f*, *h*, and *k*) were taken during rewarming after exposures to much lower temperatures. Both rows show the atrioventricular dissociation and inverted P waves which are characteristic of hearts at very low temperatures.

The first record was made before the first exposure to 2 C (compare fig. 1, 3*a*). On it, the QRS complex is both low and broad (fig. 3*a*). The time occupied by the QRS complex which is commonly called "ventricular activation time" has been shown to be the time required for depolarization of the myocardium.[4] Therefore, a broad QRS complex

TABLE 2.—*Effects of Cooling and Rewarming on Heart Rate, Beats per Minute*

Temperature	1st Period		2nd Period		3rd Period		4th Period		5th Period	
	Cooling	Warming	Cooling	Warming	Cooling	Warming	Cooling	Warming	Cooling	Warming
16 C	40	54	29	35	44	29	22	16	20	8
14 C	20	45	24	24	44	16	18	10	12	12
12 C	16	50	24	12	32	10	14	8	10	8
11 C	15	36	20	12	...	4	12	6	9	5
10 C	12	30	20	8	24	...	12	2	8	3

indicates slow depolarization and a narrow one, rapid depolarization. As mentioned above, low potentials appear to be associated with poor condition of the heart muscle and high potentials with good condition.

Difficulties were encountered with perfusion during the second cooling period. These were reflected in the height of the waves (fig. 3*c* and *d*). Nevertheless, the rate of ventricular depolarization, as indicated by the breadth of the QRS complex, was more rapid than it had been before the first cooling period, 1 hour and 52 minutes earlier (compare fig. 3*a*). Depolarization time 3 hours and 22 minutes after birth was 0.06 seconds (fig. 3*c*). From this it increased until, 11 hours and 37 minutes after birth, it was 0.8 seconds (fig. 3*g*). A considerable degree of recovery was noted after the first exposure to 0.1 C, and 16 hours and 23 minutes after birth depolarization time was reduced to 0.36 seconds (fig. 3*j*).

In contrast to the records of the upper row, those of the lower row were made as the fetus was rewarming after a period at greatly reduced temperature. Important differences are seen when the records in the lower row are compared with those directly above. The QRS complexes of the lower row are taller and narrower than are those of their counterparts above. This is most noteworthy at figure 3*b* and least obvious at 3*d*. At figure 3*d*, as well as at 3*c*, blood was not flowing through the perfusion cannula at the time the record was being taken.

The recovery of the heart illustrated at figure 3*d* was the most remarkable of the series and was typical of the entire course of the first rewarming period. Until the temperature of 2 C was reached, the tracings during the cooling phase of the first period in no way foreshadowed the great increase in rate and amplitude which characterized all temperatures through 15 C during the first rewarming. At 2 C a slight elevation in potential over that in earlier records was noted. This increased steadily, until at 11 C it reached a maximum of 1 mv. At higher temperatures it diminished somewhat. The increase in heart rate which accompanied the increase in temperature likewise was more marked during the first rewarming period than in any subsequent one. As noted earlier, the maximum heart rate was not reached until the temperature was 16 C.

At no time during the 21 hours was there a clearly recognizable wave of Osborn, which was first seen in hypothermic dogs [5] and has been subsequently described for hypothermic adults, including man. Notching of the R wave, which has been emphasized by Nardone [6] as a concomitant

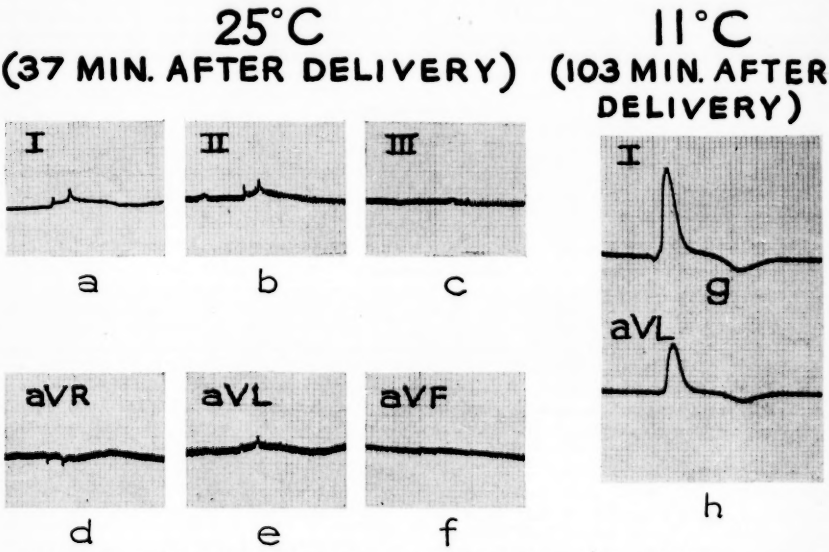

Fig. 2.—Comparison of electrocardiographic tracings at 25 C and 11 C. Rate: 1 mm.=0.04 seconds; gain: 1 mv.=20 mm.

of low temperature, is seen in figure 3*e* and particularly in 3*j*. As may be seen by comparing figure 3*e* with 3*f* and 3*j* with 3*k*, it is a reversible change.

Increasing width of the QRS complex with the passage of time is to be seen in both the upper and lower rows of records. This slowing of depolarization was not a completely irreversible one, however. Between figure 3*g* and 3*h* the time for the QRS complex was reduced from 0.7 seconds to 0.4 seconds after an exposure to 0.1 C. Although slowing of the QRS complex accompanied the reduction in heart rate which was observed at each temperature with the passage of time, its exact significance is problematical. The possible significance of this and other aspects of the ECG will be considered later.

Comment

This 580-Gm. fetus appears to have established several records for survival. There have been no published records of maintenance of heartbeat for more than 12 hours in apneic infants even with perfusion.[7] In addition, there are apparently no previous reports of recovery of heart action in adults, infants, or human fetuses from temperatures below 16 C. Laufman has reported one case of an adult whose temperature was 18 C 90 minutes after admission.[8] Extrapolation of the temperature recovery curve indicates that the patient's temperature was 16 C on admission. Dammann and Muller[9] have reported cooling a newborn infant to 11 C and obtaining recovery of heart action at about 20 C with the aid of massage. However, as the temperature rose above 26 C, the child became progressively worse, and recovery was not permanent. The heart of the fetus reported on here not only continued to contract at temperatures down to 0.1 C but, after two periods of asystole at that temperature, recommenced spontaneously on being rewarmed.

Length of Apneic Survival.—The studies of Enhörning and Westin provide a standard of comparison for the effectiveness of deep hypothermia in premature infants. In fetuses maintained at 37 C without perfusion, heartbeats have been recorded for a maximum of 93 minutes. At this temperature, perfusion with oxygenated blood increases cardiac survival only slightly. At 25 C heartbeat may continue for three or four hours without perfusion. Successful perfusion at this temperature increases survival time by a factor of three or four.[7]

In the case reported here, in spite of intermittent and largely ineffectual perfusion, contractions were maintained for a much longer period. In addition, when the autopsy was performed 23 hours after delivery, exposure of the heart to air was followed by a number of contractions of the ventricules before cardiac activity ceased altogether. During the two-hour interval between termination of the experiment and autopsy, the fetus had been exposed to a sixth period of deep hypothermia, since it had been left in the solution at 2 C.

Although there appear to have been no reports of measurements of oxygen uptake of fetal hearts at 37 C, if one may assume that their energy requirements per contraction are of the same order of magnitude as those of adults, an estimation may be made of the effectiveness of 300 ml. of oxygenated blood. At 37 C the adult heart uses about 0.097 ml. of oxygen per gram per minute or 5.8 ml. per hour.[10] Since the heart of a 580-Gm. fetus weighs 5 Gm. and beats at twice the rate of the adult heart, this places its normal hourly requirements at 58 ml. of oxygen. At saturation 300 ml. of adult blood contains 60 ml. of oxygen. However, before reaching the fetal heart a portion of the blood entering the abdomen in the umbilical vein passes through the large left lobe of the liver.

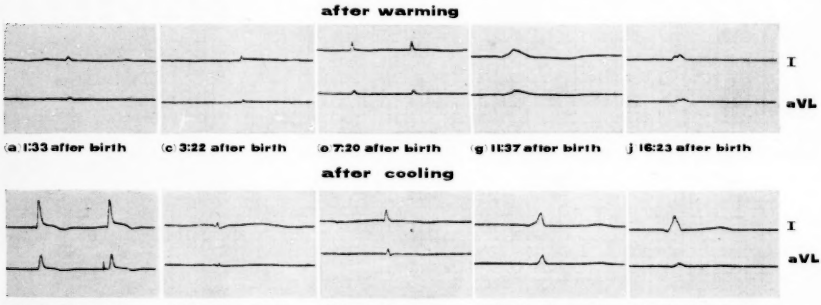

Fig. 3.—Electrocardiographic tracings at 11 C. Rate: 1 mm. = 0.04 seconds; gain: 1 mv. = 20 mm. (32% of original size).

Under hypoxia, this might be expected to take an appreciable toll of oxygen from the blood. In addition, only about 5% of the blood passing through the heart reaches the myocardium via the coronary system.[11] On the other hand, it must be borne in mind that, because of its thin walls, the fetal heart is less dependent on coronary circulation than the adult, because a larger fraction of its needs can be supplied by diffusion from the lumen. Equating these various factors, it appears likely that 60 ml. of oxygen in the umbilical vein could not have supplied the normal requirements of the heart at 37 C for more than approximately 15 to 30 minutes.

That total failure of the heart was so long postponed is attributed chiefly to the extremely low metabolic requirements during the 13½ hours that it was below 10 C, and particularly in the 9½ hours it was below 5 C. Fitzgerald [11] has reported a sharp fall in oxygen consumption of newborn mice below 10 C and particularly from 4 C downward. At 2 C they utilized only one-sixteenth the oxygen needed at 10 C. That a similar condition obtains in the premature human infant is suggested by the observation that the blood in the cutaneous vessels became fiery red during the periods when the fetus was packed in snow (at temperatures below 4 C). This indicated that the metabolism of the tissues was so low that sufficient oxygen diffused from the air to supply their needs and saturate the blood also.

Possible Role of Carbon Dioxide.—Although no measurements of blood oxygen or carbon dioxide were made, the presence of varying degrees of cyanosis at all times except during the two periods below 2 C is evidence of hypoxia and, associated with it, of hypercapnia. This may have contributed to the long survival of the heart of the fetus. A number of investigators have shown that it is possible to revive high percentages of mice, rats, hamsters, dogs, and monkeys from temperatures near 0 C by exposing them during cooling to hypercapnia.[12] Although hypoxia is not absolutely essential,[12b] for mice, at least, a combination of the two produces higher percentages of complete recoveries than when carbon dioxide alone is used.[13]

Carbon dioxide has several physiological effects which are beneficial in hypothermia. It reduces oxygen uptake and heat production, thereby aiding in cooling. It suppresses shivering, which elevates the oxygen requirements as much as 400%. Of even greater possible value in deep hypothermia is its well-known effect as a vasodilator, particularly of the cerebral arteries. Severe vasoconstriction is a well-documented accompaniment of deep hypothermia and may well be responsible for the damage which has been noted, from both behavior changes and histological preparations, in animals kept hypothermic for long periods.[2b]

It is possible likewise that the heart of the fetus might have developed asystole earlier if there had been no periods of rewarming or if the temperature of 0.1 C had been maintained for more than one hour. Animal experiments have disclosed a critical period between one and two hours at this temperature. In the mouse, arterial vasoconstriction takes place during this period even though the cooling is accompanied by hypercapnia.[14]

General Implications.—The primary effect of hypothermia on cells is a reduction in the rate of chemical activity which becomes more pronounced with each degree that the temperature is lowered. This makes temperatures between 10 C and 0 C especially attractive for those interested in protecting vital organs from oxygen lack. There is no theoretical reason why temperatures down to zero should not be tolerated.

In the case of the adult, secondary effects induced by hypothermia constitute serious limitations to its use. The most serious of these result from reactions of the vascular system to cooling. Ventricular fibrillation and arterial vasospasm are two of the worst of these.

As indicated by studies on fetuses of other mammals, these secondary effects apparently do not constitute as serious a problem in the case of the newborn infant. The fetal ventricle exhibits little tendency to fibrillate; although the lowest limits from which recoveries have been reported vary, they are regularly lower for the newborn infant than for the adult of the same species.[2b]

The asphyxiated fetus would appear to be an ideal subject for treatment with hypothermia. On the one hand, mild asphyxiation increases the tolerance of cooling, and, on the other, the reduced metabolism at low temperatures protects the cells of vital organs from death caused by severe asphyxia. There appears to be no rational basis for the use of heat as part of the treatment of asphyxia. Indeed, animal experiments have shown that with no other treatment than reduction of body temperature there is 100% spontaneous recovery from exposures to asphyxia which are 100% lethal for warmer littermates.[2a]

The results of the present study suggest that the 580-Gm. human fetus more nearly resembles the newborn mouse or rat than the newborn guinea pig in its ability to tolerate deep hypothermia. About half of the guinea pigs die at 10 to 12 C,[2a] whereas newborn rats recover spontaneously from 1 C.[15]

The fact that heart action continued at temperatures below 1 C does not in itself constitute an indication for the use of hypothermia. However, the improvement in heart action after the periods of lowest temperature is evidence of its benefits. This fact strengthens the argument that, when given an adequate test, hypothermia will prove

to be able to protect both the life and the brain of the asphyxiated newborn human infant as it has been shown to do in the neonatal guinea pig.[2]

Summary

Cardiac activity was maintained for 21 hours in an apneic 580-Gm. (1.25-lb.) female fetus. During this period, the fetus was perfused with 300 ml. of oxygenated blood and kept at deep colonic temperatures between 22 C and 0.1 C. For more than 17 hours the temperature was below 15 C, and for nearly 2½ hours it was below 1 C. On five occasions the temperature was reduced to 4 C or less, and during the last two cooling periods it reached 0.1 C.

Electrocardiograms showed that heart activity did not cease until the temperature fell to 0.1 C and that it recommenced spontaneously on rewarming. A comparison of the records at 11 C showed that after the periods of deepest hypothermia there was an increase in the height (increase in voltage) and a narrowing (increase in rate of ventricular depolarization) of the QRS complex. This was most striking after the first cooling period, when the QRS complex reached a maximum of 1 mv. However, even after the fifth period 0.5 mv. was recorded. At the beginning of the study the voltage was 0.01 mv. at 25 C.

This appears to have established a record both for the lowest temperature during which cardiac activity has been recorded and the lowest temperature from which spontaneous recovery of heart beat has been observed. Also established is a record for the longest time during which heart beat has been reported in a perfused human fetus. This shows that the heart of the premature infant will tolerate far lower temperatures than previously thought possible.

This study was aided by grants from the National Institutes of Health and Association for the Aid of Crippled Children.

Dr. John Lind provided material and facilities for this study.

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RING DERMATITIS.—During the past five years, many patients have been patch-tested with metals. Every so often there would be seen a dermatitis of the ear lobes, back, neck, chest, shoulders, wrist, or lower abdomen where metal contact presupposed a metal sensitivity. The diagnosis seemed so obvious that it was recorded. When patch tests were performed, the diagnosis was not confirmed. A greater range of test solutions were made up, and these, too, failed to confirm the presence of any metal sensitivity. Patch tests were done adjacent to the area of dermatitis without positive results. Testing solutions were dropped on the patch of dermatitis without the slightest indication of an aggravation. It thus seems that a dermatitis from contact with metal, in the presence of negative patch-test results, may well be a primary irritation from the action of skin-surface salts on metals and/or alloys.—L. E. Gaul, M.D., Ring Dermatitis, *A. M. A. Archives of Dermatology*, May, 1958.

EFFECT OF TRANQUILIZING AGENTS ON RADIOACTIVE IODINE UPTAKE IN THE THYROID GLAND

Morris T. Friedell, M.D., Chicago

There are many patients who arouse clinical suspicion of having hyperthyroidism yet who do not suffer from true thyrotoxicosis. These patients usually have no enlargement of the thyroid gland and lack the true eye signs of toxic diffuse goiter (Grave's disease). They are nervous and insomnic, complain of palpitation of the heart, and have some degree of tachycardia. They may or may not show evidence of weight loss and may even be obese. A routine study of 24-hour uptake of radioactive iodine (I^{131}) by the thyroid gland in these persons will often show an uptake which is in the upper normal or even in the toxic range.[1] Further studies may reveal normal thyroid function by means of such tests as conversion ratios (ratio of inorganic to organic iodine in plasma) and plasma protein-bound iodine studies. It has been shown that oral administration of thyroid extract or triiodothyronine will reduce the I^{131} uptake in persons without true thyrotoxicosis but will not greatly affect the I^{131} uptake in persons with hyperthyroidism. According to Selye,[2] stimulation of thyroid activity during periods of stress and by the stress mechanism are readily postulated. It was felt that this increase in thyroid activity might be reflected in an increase in the I^{131} uptake. It was therefore decided to test the effect of tranquilizing agents on those patients in whom elevated I^{131} uptakes were found without clinical signs of hyperthyroidism and to measure changes, if any, in the I^{131} uptake by the thyroid gland.

Methods

Patients recently seen who had had I^{131} uptake determinations which were higher than the expected normal range were requested to return for repeat examination. Those patients who volunteered to return and who were selected for this study in each case showed an elevated I^{131} uptake when the test was repeated. Determination of the protein-bound iodine to inorganic iodine ratios revealed, however, that the conversion from organic to inorganic iodine in each patient was less than 50%, thus establishing that hyperthyroidism probably was not present. A double-blind study was then carried out with three-week courses of therapy with meprobamate (Miltown), 400 mg. three times a day; meprobamate, 400 mg. fortified with 0.5 mg. of benactyzine hydrochloride three times a day; and a placebo tablet which was indistinguishable from the other two tablets. The investigators knew which was the meprobamate but not which was the meprobamate with benactyzine and which was the placebo. In so far as possible, the three groups of medicaments were administered in rotation so that each patient received all three courses of medication, but in varying order. After each course of medication, the I^{131} uptake determination was repeated.

From the Isotope Laboratory, Mercy Hospital.

Results

The results of the investigation are set forth in the accompanying table. Twelve patients were subjected to either the whole or a part of the study. The initial I^{131} uptake varied from 35 to 62% in these patients. All of the patients were women, with one exception. One patient failed to respond to treatment with the tranquilizing agents and continued to show an increase in I^{131} uptake during the course of management. This patient had had an initial conversion ratio of 46%. After three months the conversion ratio had risen to 76% and the I^{131} uptake to 63%. At this time it was felt that a diagnosis of true hyperthyroidism had to be made, and the patient was treated subsequently with I^{131}, to which she responded very well. (This case is not included in the table.)

Thyroid Radioactive Iodine (I^{131}) Uptake in Response to Treatment with Tranquilizing Agents

Case No.*	Age, Yr.	24-Hr. Uptake, %			
		Initial	After Placebo	After Meprobamate	After Meprobamate and Benactyzine
1	30	62	34		20
2	58	46	37	30	28
3	20	52	58		
4	51	49	49	41	
5	40	42	36	7	9
6	40	38	53		
7	41	35	35	35	35
8	50	41		32	
9	20	41		35	
10	25	56	48		28
11	26	62	43	40	23
12	44	62			38
Av.		49	44	33	26
Median		49	43	35	28

* All patients were female except that in case 12.

Nine patients did not respond to the medication with the placebo, and the I^{131} uptake was either materially unchanged or higher after completing the medication for three weeks with the placebo tablets. In two patients the administration of placebo tablets had to be discontinued since the patients did not feel that any improvement was being obtained from them. The response to the meprobamate alone in eight patients was generally satisfactory, although in three instances the reduction in I^{131} uptake was not considered to be significant.

In six patients the response to the meprobamate and benactyzine combination was extremely satisfactory. There was reduction of the I^{131} uptake in almost each instance to below 30%. Interesting was the case of the male patient who had been treated two years prior to this study for true hyperthyroidism with radioactive iodine. After this treatment he had remained well for a period of two years, at which time he returned because his symptoms of nervousness and his "jittery" state were similar to what he had experienced while suffering from thyrotoxicosis. His I^{131} uptake, which had been followed closely during the past two-year period, had ranged around 40%. At the time of the study it had risen to 63%. After a three-week course of meprobamate plus benactyzine, the I^{131} uptake fell to 38% and there was no subjective evidence of nervousness or other symptoms of excitement.

Comment

From these results it appears evident that the tranquilizing agents can reduce the I^{131} uptake of the thyroid gland. The locus of this effect, of course, was not established by this study. There is no reason to suspect that it is due to a direct chemical effect on the thyroid gland, such as occurs with the antithyroid drugs (thiouracils), nor does the effect seem to be similar to that of administered thyroid extract, with which there is a reduction of I^{131} uptake by the thyroid gland in those patients in whom true clinical hyperthyroidism does not exist. The reaction of the tranquilizing agents indicate that meprobamate shares the central interneuronal blocking action of mephenesin but has an action of much longer duration.[3] The drug appears to be a mild hypnotic and tolerance does not appear to develop. Addiction and toxicity have been reported to be low.

The in situ action in the central nervous system is not yet understood, although it appears to be useful in the treatment of alcoholism and anxiety and tension states. It is possible that the reduction of the tension state would have some secondary or other effects on the demands on the thyroid gland, such as in the stress mechanism as postulated by Selye.[2] However, confirmation exists that the tranquilizing agents do not have an effect on the activity of the thyroid gland in the presence of true hyperthyroidism or thyrotoxicosis. There is no reason to suspect that the effect on the thyroid gland could be produced by the small doses of I^{131} administered in the tracer tests, which would total less than 100 μc for each patient.

Summary

In a group of patients in whom the radioactive iodine (I^{131}) uptake was elevated without clinical evidence of hyperthyroidism and in the absence of enlargement of the thyroid gland but in whom there were signs of nervousness and excitement which exist in a chronic tension state, the effect of tranquilizing agents on the uptake of I^{131} was studied. The results in 12 patients who were subjected to a double-blind study indicate that tranquilizing agents, particularly meprobamate plus benactyzine hydrochloride, may sufficiently reduce the effect of tension or anxiety mechanisms on the endocrine system to effectively decrease the thyroid activity as measured by the uptake of I^{131}.

104 S. Michigan Ave. (3) (Dr. Friedell).

The meprobamate used in this study was supplied as Miltown by Wallace Laboratories, New Brunswick, N. J.

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RHEUMATIC FEVER AND THE WILLOW TREE.—Therapeutic advances are seldom the product of logical reasoning. They are more commonly the result of haphazard empiricism, often based on false assumptions. The use of salicylates in the treatment of rheumatic fever by Maclagan in 1876—a story Langdon-Brown enjoyed telling, for it appealed to his sense of the ironic—is the classic example of how progress in treatment is made. Maclagan believed that, in the orderly Victorian universe in which he lived, the natural remedy for each disease was to be found where that disease was prevalent. Noting the frequency both of rheumatic fever and of the willow tree in marshy country, he was led to use the salicin obtained from the second in the treatment of the first. After the first empirical leap in the dark, progress comes from working backwards, analyzing the reasons for success, and building upon this more solid foundation. It will be seen that the chemotherapy of malignant disease is following this traditional pattern, and its theoretical basis is largely derived from a rationalization of its successes.—R. B. Scott, D.M., F.R.C.P., The Chemotherapy of Malignant Disease, *British Medical Journal*, Jan. 4, 1958.

ACUTE BLOOD LOSS REQUIRING FIFTY-EIGHT TRANSFUSIONS

USE OF ANTIGRAVITY SUIT AS AID IN POSTPARTUM INTRA-ABDOMINAL HEMORRHAGE

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and
Donald F. Dohn, M.D., Cleveland

In this case of placenta percreta (a placenta that has grown through the uterine wall because of failure of development of decidua basalis), control of bleeding was finally accomplished after a desperate struggle in which the application of pneumatic pressure to the lower half of the body appeared to mark the turning point.

The modified antigravity suit (commonly referred to as the "G-suit") used in this case was developed primarily for the purpose of preventing postural hypotension during neurosurgical operations with the patient in the sitting position.[1] It consists of a large plastic inflatable bladder that is wrapped about the lower half of the body after the manner of a huge blood pressure cuff. This principle was first employed in 1903 by Crile [2] for the prevention and treatment of hemorrhagic shock in surgery of the head and neck. As blood transfusions became relatively safe it was abandoned, to be reapplied many years later in the era of high-speed flying.

958
167

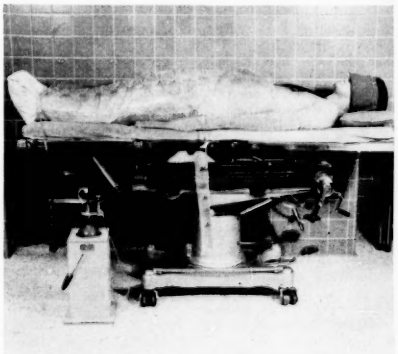
Report of a Case

A 36-year-old woman, gravida 6, para 3, in her sixth month of pregnancy, was delivered of a stillborn fetus while she was under spinal anesthesia. Delivery was followed by a frightening gush of blood and an immediate state of shock. Manual exploration revealed the upper half of the placenta to be completely detached from the anterior uterine wall, while its lower half, extending downward to the internal os, was tightly adherent. The separated part of the placenta was removed manually and efforts to separate the adherent portion were abandoned when it became apparent that this was an instance of placenta percreta. The uterus was firmly packed, fluids were administered intravenously, and a blood transfusion was given. The patient rallied as preparations were being made for an abdominal hysterectomy.

The abdominal cavity was opened by lower midline incision with the patient under cyclopropane anesthesia. An area 20 cm. in diameter involving the anterior wall of the lower uterus resembled the fetal surface of a placenta. The intrauterine pack was removed per vaginam and the patient again went into shock. It was decided that hysterectomy should be performed immediately, and as the bladder reflection was incised, placental tissue was encountered. There was no anterior uterine wall, the placenta having completely invaded and replaced the myometrium, and there was no cleavage plane between placenta and bladder. Hysterectomy was followed by troublesome bleeding from the remaining placental tissue, finally controlled by figure-of-eight sutures, oxidized cellulose (Oxycel), and the pressure of the advancement of the bladder over this oozing area. Closure was completed four hours post partum, by which time the patient had received 11 units of blood and 3,000 ml. of 5% dextrose in water. With phenylephrine (Neosynephrine) hydrochloride added to the intravenously given fluids, the blood pressure was 110/50 mm. Hg and the pulse rate was 130.

Despite the continued intravenous administration of citrated blood and of fluids containing vasoconstrictor agents, the blood pressure gradually fell to 70/60 mm. Hg. The abdomen became distended and tympanitic; respiratory embarrassment and ashen pallor ensued. It seemed obvious that massive intra-abdominal hemorrhage had occurred.

Seven hours after hysterectomy the abdomen was reopened. An estimated 3,500 ml. of clotted and liquid blood was removed from the peritoneal cavity, 1,000 ml. of which was filtered and retransfused. With the table in the shock position, the patient was receiving infusions of blood or fluid into four veins simultaneously. The chief sources of bleeding appeared to be the spongy mass of placental tissue beneath the bladder, the stumps of the broad ligaments, round ligaments and tubes. These were quickly religated with figure-of-eight sutures, the pelvis was packed, and a unit of blood was given into the aorta. With removal of the packs, bleeding continued. The right internal iliac artery was tied off, temporary ligatures were placed on both common iliacs, and the pelvic and vaginal packs were reapplied, but to no avail. As the patient was receiving approximately her 30th transfusion, the rate of bleeding increased and hemolysis became evident by inspection of the urine. In an attempt to restore platelets and other elements lost from the circulation, the patient was given 2 units of fresh blood by direct transfusion, 3 units of fibrinogen, a unit of serum albumin, 3 Gm. of calcium gluconate, and hydrocortisone.



G-Suit is placed beneath the patient, folded over him, and laced snugly. Gas enters through a tube at one end. Desired pressure is maintained by escape valve shown hanging from table. This is filled with water to desired level. This pressure cannot be exceeded as excess gas escapes by bubbling through water.

From The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute.

After six hours of operating time the prognosis appeared hopeless. Therefore, nine large packs were placed in the peritoneal cavity, the incision was closed snugly over them, and the patient was returned to her bed. Sand bags were placed on the abdomen, the legs were wrapped with elastic bandages, and the foot of the bed was elevated on shock blocks. Within 18½ hours of delivery, the patient had received 55 units of blood, which included the 2 units recovered from the peritoneal cavity and the 2 units of uncitrated platelet-containing blood given by direct transfusion. While 2 additional units of citrated blood were running in, the blood pressure taken with the patient in the shock position was 86/62 mm. Hg and the pulse rate was 144.

At this juncture, in an effort to accomplish more effective compression of the bleeding area, the G-suit was wrapped about the patient so as to encompass her from the ankles to the epigastrium and was inflated to 20 mm. Hg. The patient aroused and complained of her head-down position as the blood pressure rose to 104/72 mm. Hg. The shock blocks were removed and the pressure fell to 96/76. The rate of transfusion was slowed and the pressure gradually rose to 114/80 while the pulse rate increased to 160. Twenty-four hours post partum, after the administration of one additional unit of blood, the pulse rate began to decrease. The 24-hour output of urine was 415 ml. Thirty-six and one-half hours after delivery, and after the patient had been in the G-suit for 18 hours, the blood pressure stabilized at 130/78 mm. Hg, and the pulse rate at 130. Six hours later the G-suit was deflated and removed with no significant change in the pulse rate or the blood pressure.

Eighty-three hours after delivery the abdomen was opened for the third time, a quantity of blood was evacuated, and the abdominal and vaginal packs were removed. This was followed by no further bleeding, and the vital signs remained stable. The subsequent hospital course was marked by ileus, pulmonary atelectasis, fever, jaundice, and a left subphrenic abscess. The patient was discharged on the 54th hospital day; subsequent convalescence was uneventful except for a mild episode of hepatitis which developed on the 129th day. There were no cerebral symptoms at any time aside from a mild instability on walking, which cleared completely within six months.

Comment

When the G-suit was applied 18½ hours post partum, after two lengthy and apparently futile abdominal operations, the patient had received 10,000 ml. of fluid with other restorative measures, and was receiving her 56th and 57th units of blood. During the first few hours in the G-suit she received 1 additional unit of blood, making a total of 58 units within 24 hours. No more blood was needed. Among the many doctors who attended this patient, there is some division of opinion as to whether the final control of bleeding was due chiefly to the use of the G-suit, the intra-abdominal packs, the 2 units of fresh uncitrated blood, or to prayer.

The patient's blood was type O, Rh+ and she received only type O, Rh+ donor blood throughout the ordeal. The supply of banked blood was rapidly exhausted in this emergency and thereafter the citrated blood that she received, still warm from the donor, probably contained a goodly number of platelets. She was given 29,000 ml. of blood within 24 hours. To our knowledge this is the largest quantity ever administered within this period of time. Artz, Sako, and Bronwell [3] have reported a Korean battle casualty to whom 23,350 ml. of blood was given within 24 hours.

As a result of the above experience, the G-suit was used in another case of postpartum hemorrhage in which 20 transfusions were required within 20 hours to combat hemorrhagic shock. In this case also, after application of the G-suit, only 1 additional unit of blood was required to restore and maintain the blood pressure level.

2020 E. 93rd St. (6) (Dr. Gardner).

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THERAPEUTIC USE OF CORTICOTROPIN AND CORTICOIDS.—In the presence of any inflammatory or allergic reaction that proves limiting to the well-being, activity and long-range plans of the patient, the use of corticoids or corticotropin should be considered. However, at all times one must remember that corticoid therapy is only symptomatic and that its effectiveness is due largely to inhibiting the bodily defense mechanisms and minimizing their immediate and long-range destructive effects. As the body defenses are, of course, in general beneficial, such therapy is always a calculated risk and the indications are only relative. Only in substitution therapy is there an unequivocal indication. Here one attempts to reproduce physiologic levels of corticosteroids when the adrenal cortices are not functioning normally, rather than to produce pharmacologic effects by corticoid levels in excess of normal. In all other conditions one must weigh the benefits derived from the partial control of the manifestations of a given disease with the inevitable side effects that accompany the use of these agents when used for their pharmacologic effect.—V. C. DiRaimondo and P. H. Forsham, Pharmacophysiologic Principles in the Use of Corticoids and Adrenocorticotropin, *Metabolism*, January, 1958.

FATAL JAUNDICE ASSOCIATED WITH IPRONIAZID (MARSILID) THERAPY

REPORT OF A CASE

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Iproniazid, a derivative of isoniazid, has recently been introduced as a "psychic energizer." The drug was originally investigated for its antituberculous properties, but the central nervous system stimulation noted in many patients, greater than that obtained with the parent compound, led to its present use. A number of neurological and autonomic disturbances, mostly relatively mild, have occurred in many patients receiving the drug and have been well described.[1] A more serious and less well-known toxic effect of the drug is its action on the liver.

Abnormal liver function test results, developing in the course of iproniazid therapy, were reported in 9 out of 52 patients in whom such tests were done.[2] All returned to normal on the same, or decreased, dosage or on withdrawal of the drug. Out of another group of 30 patients receiving iproniazid,[3] 3 developed transient sulfobromophthalein (Bromsulphthalein) retention. In a series of 142 patients treated with the drug,[1] 4 developed jaundice, all with subsequent recovery. Of these patients, the jaundice of one was in all probability due to anatomic factors unrelated to iproniazid therapy; since the other patients had all received multiple transfusions, a clear-cut relationship to the drug could not be definitely established. A fifth case of jaundice, ending with a fatal necrosis of the liver, has recently been reported in one patient of a series of 31 receiving the drug,[4] and we are aware of another patient who became jaundiced and died shortly after stopping a two-month course of therapy with the drug, and who, on postmortem examination, showed a generalized necrosis of the liver.[5] This case occurred in a large hospital in New York City, and exposure to other known hepatotoxins, including contaminated blood, could reasonably be excluded. It is the purpose of the present paper to present another case of fatal jaundice in association with iproniazid therapy.

A 47-year-old male was first seen in this hospital on Dec. 2, 1957, presenting with the picture of jaundice and hepatic coma. His history included a myocardial infarction three years earlier, with frequent chest pain since, for which he had been treated with a variety of coronary vasodilators, the most recent having been pentaerythritol tetranitrate and choline theophyllinate. He had had vague intermittent epigastric distress for a long time, for which he had been given antispasmodics, but he had never had any documented gastrointestinal tract pathology (except for a rectal polyp removed two months previously). There was no history of allergies, of jaundice, or of known hepatic or renal disease. His alcoholic intake had always been low, and he had had no blood transfusions. For over a year prior to his present illness he had been nervous and depressed and had been treated with a variety of sedative and tranquilizing drugs, including phenobarbital, reserpine, perphenazine (Trilafon), and chlorpromazine. He had taken no chlorpromazine for at least six months prior to his present illness, according to his local physician. All other drugs except the coronary vasodilators were discontinued about two and a half months prior to admission, at which time he was started on therapy with iproniazid, 150 mg. per day. He was instructed to reduce this dosage to 100 mg. or less in a few weeks, although his compliance with this instruction is uncertain, since he found the drug so beneficial in alleviating depression. He stated that no other drug had given him an equal sense of well-being, a condition which lasted, under continuous treatment with iproniazid, until two weeks before admission, when he began to be aware of anorexia and fatigue. He went to his local physician, who could find nothing unusual, and specifically no enlarged liver. Four days later the patient noted dark urine and early signs of jaundice. These symptoms were followed in a day or two by frequent, nonbloody vomiting, dull pain in the right upper quadrant, and progressive weakness. One week before admission he had a palpable, tender liver, with obvious jaundice, 4+ cephalin flocculation, 4+ thymol turbidity, and normal alkaline phosphatase and cholesterol levels. Shortly before admission it had become impossible to feel the liver, and the patient had become more deeply jaundiced, markedly drowsy, and at times disoriented.

On admission to the hospital the patient was a well-developed, somewhat obese male, extremely jaundiced, somewhat confused, and frequently disoriented. His temperature was 98.6 F (37.0 C), pulse 86, respirations 14, and blood pressure 110/70 mm. Hg. The remainder of the physical examination was normal. There was no tremor, and the liver was not palpable.

Laboratory results were as follows: The hematocrit was 52%, the hemoglobin level 17.2 Gm. per 100 cc., the white blood cell count 19,400 per cubic millimeter (polymorphonuclear leukocytes 80%, lymphocytes 16%, monocytes 3%, and basophils 1%), and the platelets were diminished, as seen on a smear. The urine was dark brown and strongly positive for bile, with a specific gravity of 1.012, albumin 1+, glucose 1+, with two to three red blood cells and two to three white blood cells per high-power field, and occasional granular bile-stained casts. The erythrocyte sedimentation rate was 3 mm. per hour, and the carbon dioxide content of the blood was 12.8 mEq. per liter. The sodium content of the blood was 141 mEq. per liter and the potassium and chlorine content 4.9 and 103 mEq. per liter respectively. The blood sugar level was 89 mg. per 100 ml., blood urea nitrogen level 13 mg.%, prothrombin time 29

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seconds (normal is 15 seconds), cephalin flocculation and thymol turbidity both 4+, and the bilirubin level 30.4 mg.% (direct). The total cholesterol level was 83 mg.% (19% esterified), and the serum ammonia concentration was 140 mcg.%. The patient's blood culture was negative. Gastric aspiration yielded 4+ blood by the guaiac test. A chest x-ray made with a portable machine was normal. The electrocardiogram showed evidence of an old posterior myocardial infarct.

Despite intensive therapy with intravenously given fluids, antibiotics, and finally steroids, the patient had a rapidly downhill course with fever, tachycardia, increasing disorientation, hypotension, and finally death 24 hours after admission. His serum ammonia level rose to 364 mg.% preterminally.

At autopsy the patient was found to have a normal-sized liver, which on microscopic section showed massive necrosis of liver cells, with some preservation of architectural framework. The sinusoids were congested, especially about the central veins, while the bile ducts were normal. Inflammatory cell infiltration, predominantly of the chronic variety, was noted, together with areas of regenerating liver and bile duct cells. The kidneys were congested and edematous and showed focal hemorrhages into the pelvic fat. An occasional distal convoluted tubule showed early necrotic changes, and several bile plugs were noted in the tubules. The stomach contained some gross blood but was normal on gross and microscopic section. The heart showed evidence of an old posterior infarct of the left ventricle. The remainder of the examination, including that of the central nervous system, was essentially normal.

Comment

A 47-year-old man who had been on therapy with iproniazid, 150-100 mg. a day, for about two and one-half months died with fulminating jaundice and the picture of acute yellow atrophy of the liver. The only known hepatotoxic drug he had received, chlorpromazine, had been withdrawn six months previously. It is not claimed that iproniazid was definitely the toxic agent, since this illness could have represented an infectious hepatitis. It is also possible, though unlikely, that an injection with a poorly sterilized needle at the time of his rectal polypectomy two months previously could have transmitted serum hepatitis. Nevertheless, it is noteworthy that iproniazid has been associated with transient abnormalities of liver function in a moderate number of patients in whom these tests were made, that one case of death due to necrosis of the liver in a patient receiving the drug has already been reported, and that another unpublished case is known to exist. The jaundice appears to be a hepatocellular, rather than an obstructive, type. Serious consideration should be given to this potentially severe form of toxicity in a relatively new drug.

620 W. 168 St. (32).

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ANTIMETABOLITES AS DRUGS.—The introduction of the antimetabolite concept into pharmacology seems to be causing such a change in thinking about the mode of action of drugs that a revolution may be said to be in progress. Perhaps one of the most significant aspects of this revolution is that reliance on chance for the discovery of the first member of a new series of useful agents is being broken. It is now becoming possible to predict the chemical structure of the first member of a new series and to see these predictions come true. This is not to say that the end of chance discovery and of empiricism is just around the corner. Many more great discoveries will undoubtedly be made this way in the future, just as they have been made in the past. . . . What has been added by the antimetabolite concept is the knowledge of how to interpret a chance discovery of this sort and how to proceed to the next logical step. The antimetabolite concept depends for any of its successes on the accumulated knowledge of fundamental physiology and biochemistry. We must know what substances are important in particular bodily functions. We must know what the signs of deficiency of each of these essential metabolites are. Also, in the present state of infancy of the concept, we must often rely on a lucky conjecture. We must feel, therefore, that all reliance on chance has not been discarded but that we have been able to advance a little way.—D. W. Woolley, Ph.D., M.D., The Revolution in Pharmacology, *Perspectives in Biology and Medicine*, Winter, 1958.

PERIVENTRICULAR CALCIFICATION AND CYTOMEGALIC INCLUSION DISEASE IN NEWBORN INFANT

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and
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The purpose of this case report is to call attention to the unusual findings on the skull roentgenograms of a newborn infant. The films disclosed calcium lining the walls of the lateral ventricles of the brain. Such a picture has been reported four times previously,[1] all in infants with generalized cytomegalic inclusion disease. Our patient showed the characteristic cells of cytomegalic inclusion disease in the urine. We are presenting this case to suggest that this radiographic finding, when present, indicates a diagnosis of cytomegalic inclusion disease and may be pathognomonic of the disease.

Report of a Case

History.—An infant (fig.1) was born July 17, 1957, after a 40-week gestation. He weighed 2,154 Gm. (4.7 lb.) and therefore was transferred to the premature nursery at the Jackson Memorial Hospital for care. He was the first child of a 20-year-old primipara whose blood was group A and Rh positive and whose serologic test for syphilis was negative. The mother was born and reared in Puerto Rico. The pregnancy had been uneventful, with a normal spontaneous delivery. The infant cried spontaneously at birth but was noticed to have a small head.

Physical Examination.—At the time of the initial examination the infant was active, with a good color and a high-pitched cry. He was not icteric, and no petechiae or ecchymoses were seen. The calvaria appeared small in relation to the face and the size of the body. The bones of the calvaria overlapped slightly, and both fontanels were small. The anterior fontanel was 1 cm. in diameter and the posterior was 0.5 cm. in diameter. The skull failed to transilluminate. The eyegrounds were normal. The lungs were clear, and the heart was normal. The liver was palpable 2 cm. below the right costal margin, but the spleen was not palpable.

Laboratory Data.—The hemoglobin level was 18.0 Gm. per 100 cc. The white blood cell count was 11,100 per cubic millimeter; a differential count showed 11% band cells, 30% polymorphonuclear cells, and 59% lymphocytes. Lumbar puncture (fluid taken at the time the pneumoencephalograms were done) yielded crystal-clear cerebrospinal fluid that contained 14 cells, all mononuclear; a protein level of 149 mg.; and a sugar level of 36 mg. per 100 ml. A colloidal gold curve was 000121000. The serologic test for syphilis was negative. Sabin-Feldman dye tests done on two occasions, two months apart, on the mother's and infant's serum, were negative. These were done by the Communicable Disease center, Chamblee, Ga.

Roentgenograms of the skull showed a marked microcephalia. The bones of the calvaria overlapped. There was an unusual layer of calcification following the outline of the ventricles. No other calcification was noted. Pneumoencephalograms (fig. 2) demonstrated that the calcium deposits were periventricular and that there was marked dilatation of the lateral ventricles.

A disintegrated cell with changes indicative of those seen in cytomegalic inclusion disease was found in the urinary sediment. In order to obtain more material, a 24-hr. specimen was collected in formalin (10 ml. of formalin [37-40% formaldehyde] for each 100 ml. of urine). The entire 24-hr. specimen was centrifuged, and the sediment was smeared on clean glass slides. These preparations were stained with Harris' hematoxylin–alcoholic eosin. By this means, clear-cut examples of cells (probably from renal tubules) containing intranuclear inclusions and showing nuclear changes typical of cytomegalic inclusion disease (fig. 2, *insert*) were found. No cytoplasmic inclusions were seen.

Viral isolations were attempted from urine and mucous membrane washings from the mouth by Dr. M. Sigel, of the Virology Laboratory at the University of Miami, Coral Gables, Fla., but were unsuccessful. Complement-fixation antibody determinations were done by Dr. T. H. Weller of the Harvard School of Public Health, Boston, and by Dr. W. P. Rowe, of the National Institutes of Health, Bethesda, Md. At neither institution were the studies conclusive for the disease.

Fig. 1.—*Left*, anteroposterior view of infant's head showing small calvaria and overlapping of sagittal suture. *Right*, lateral view of infant's head showing small calvaria.

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958
167

Course.—The infant was discharged from the hospital at one month of age, weighing 2,500 Gm. (5.5 lb.), with a diagnosis of cytomegalic inclusion body disease. During his stay in the hospital he showed no evidence of jaundice or bleeding tendencies. His eyegrounds, examined at the time of discharge, revealed no evidence of chorioretinitis. His spleen was never palpable, but his liver was still 2 cm. below the right costal margin.

At 2 months of age he was readmitted to the hospital for follow-up studies. His weight was 4,255 Gm. (9.4 lb). The calvaria remained obviously small in relation to the size of the body. The sutures no longer overlapped, and there was no evidence of his developing a hydrocephalus. The hemoglobin level was 9.9 Gm. per 100 cc. without evidence of bleeding. The liver was palpable 1 cm. below the right costal margin. The spleen was not palpable. His urine sediment was reexamined for cytomegalic inclusion bodies, but none could be demonstrated on this admission. Repeat roentgenograms of the skull showed essentially the same pattern of calcium formation as was noted two months previously, at birth.

At 4 months of age, the infant began having generalized convulsive seizures and was readmitted to the hospital. The seizures were easily controlled with phenobarbital. Repeat roentgenograms of the skull showed a calcium formation in the periventricular areas similar to that noted at the time of birth. Intranuclear cytomegalic inclusion bodies could not be demonstrated in his urinary sediment on this admission. The infant has subsequently required phenobarbital therapy to control his convulsive seizures and is considered to be mentally retarded.

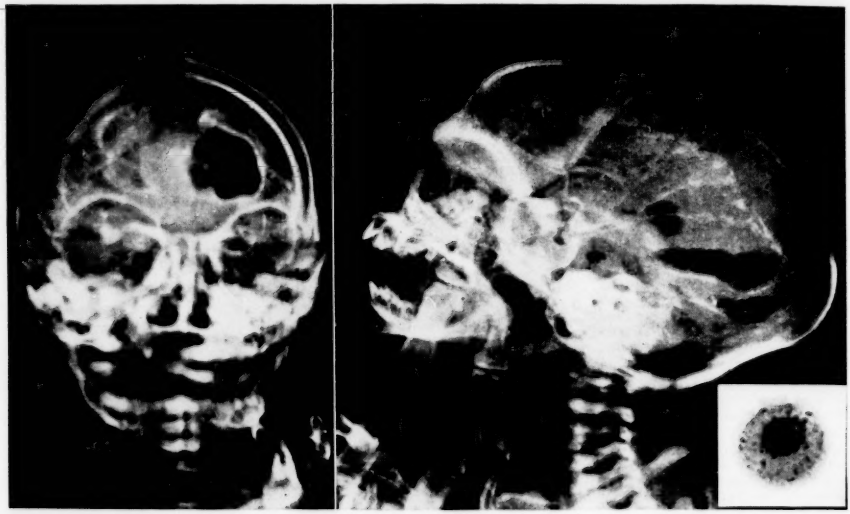

Fig. 2.—*Left,* anteroposterior view of skull showing layer of calcium lining lateral ventricles. Pneumoencephalogram resulted in filling of left lateral ventricle with air, thus making periventricular location of calcium more apparent. *Right,* lateral view of skull showing small calvaria, overlapping sutures, and periventricular calcium. *Insert,* cell, stained with Harris' hematoxylin—alcoholic eosin stain, containing intranuclear inclusion and showing nuclear changes typical of cytomegalic inclusion disease. The large dark inclusion is surrounded by fragmented chromatin.

Comment

The antemortem diagnosis of cytomegalic inclusion disease has been aided by various means: the recognition of the typical cells in hematoxylin-and-eosin or Giemsa-stained urine,[2] gastric washing,[1d] lung tissue,[3] and spinal fluid [4]; viral isolation from urine,[5] aqueous of the eye,[1d] and liver biopsy specimens [5a]; and complement-fixation [5b] and neutralization studies.[5a] The finding of the typical cells in the urine is inconstant as shown in our case and one other.[1d] The virus isolation, complement-fixation, and neutralization studies are difficult to perform, not generally available, and of varying success. The limitations of the above diagnostic aids lend emphasis to the value of a characteristic radiographic picture that may be present in some cases.

If the infant survives, the enlargement of the ventricles could result in dispersal of the calcium so that its periventricular location is no longer apparent. In such a case, the calcium could assume a "snowflake" appearance indistinguishable from the appearance of toxoplasmosis.[6] The finding of the calcium within the subependymal white matter and matrix of the lateral ventricles with sparing of

the remaining ventricular system may reflect the intrauterine age at which the disease occurred.[1b] The periventricular matrix of the lateral ventricles is still active in the late intrauterine and early neonatal life, whereas the matrix of the remaining ventricular system has reached maturity by the third month. Perhaps the disease is not contracted until after the third intrauterine month and the immature cells are most susceptible to invasion by the virus.

Summary

A case of advanced periventricular calcification in a newborn infant has been studied. Such a finding appears to be characteristic of cytomegalic inclusion disease and when present should suggest this diagnosis.

1700 N. W. 10th Ave. (36) (Dr. Daurelle).

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958
167

ACUTE INTESTINAL OBSTRUCTION.—This is the commonest serious surgical condition met with in general hospitals as emergency and taxes the surgical team to its utmost. One is confronted with a grave condition, and the entire resources of the team are required to treat the patient. It is to be noted that this otherwise fatal condition is supremely amenable to timely surgical intervention, although the incidence of mortality is still high due to poor communication, ignorance, poverty and fear causing considerable lapse of time before the patient reaches the hospital, leading to delay in diagnosis and early treatment. . . . The characteristic triad of pain, vomiting and progressive distention is almost always present, the duration varying from a few hours to a few days and in general denotes the severity of obstructive mechanisms. Absolute constipation may be an early or late sign, and may be occasionally misleading. Recurrent intestinal spasms with inability to pass flatus is almost certainly due to obstruction. In a doubtful case, positive diagnosis can be established by x-ray investigations and the approximate site of the lesion determined. . . . Intestinal intubation properly done will reduce the mortality rate particularly in the presence of adhesive obstruction. However, there is a danger in persisting with this therapy when surgical intervention is imperative. The absolute contraindications of the use of long intestinal tubes are strangulating obstruction of the small bowel and any obstruction of the large bowel. . . . The main step is the relief of obstruction by cutting the band or untwisting as the case may be. In all cases where the gut is not viable, resection and anastomosis is undertaken if the patient's condition permits. . . . Generally speaking, the patients settle down within 48 hours. A mild degree of paralytic ileus persists for 24 to 48 hours in cases of resection. Gastric suction and intravenous fluids are maintained till normal bowel movements are established. Blood transfusions are of very great value and is the best aid in correcting hypoproteinæmia and anæmia.—V. D. Kirpekar, M.S., F.I.C.S., Acute Intestinal Obstruction, *Journal of the Indian Medical Association,* April 1, 1958.

TIMESAVING AID IN HIP-PINNING

F. K. Holzwarth, M.D., Rochester, N. Y.

Anything which will facilitate the accurate and fast placing of the initial guide-wire for a Smith-Petersen nail is surely a boon, especially in poor-risk patients. For some time, it has been my custom to insert a Michel clip, after reduction and skin preparation, over the midpoint of the head of the femur.

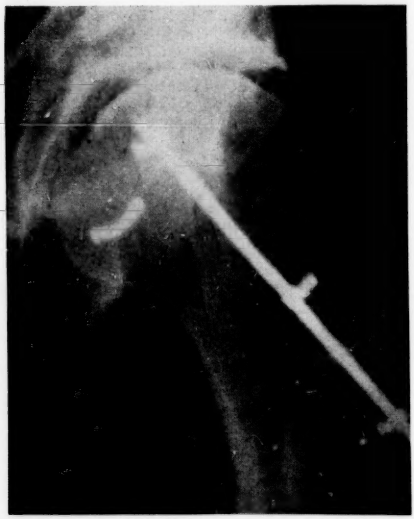


Fig. 1.—Anteroposterior roentgenogram showing guide wire lying on the skin between three Michel clips.

This point is located by palpating the femoral artery where it crosses the inguinal ligament, then moving vertically down for 1 in. and laterally for 0.5 in. Two additional clips are inserted, 0.5 in. medially and laterally to the first respectively. Ordinarily, a check x-ray is then done to ascertain the accuracy of the reduction. If it is satisfactory, the usual lateral incision and insertion of the initial guide-wire follows. The clips, plainly visible on the film, afford a target toward which to aim the drilled wire.

Frequently, the first guide-wire is not found in optimum position by x-ray. A second wire must be inserted and another x-ray taken. This consumes from 5 to 10 minutes. It has seemed possible that the time required for inserting the initial "sounding" wire might be saved by sliding a guide-wire in the loops of two clips, the one over the femoral head and the other placed at a point on the skin about 0.5 in. below the base of the trochanter major. A third clip may be added between these two to anchor the wire more securely. This wire will lie on the skin in an axis closely paralleling the midline of the femoral neck. The anteroposterior view serves as a guide in angling the first wire to be drilled into the femur and as an indicator of the depth desired to bring the point 0.25 to 0.5 in. short of penetrating the head.

The length of wire protruding lateral to the femur is then measured; the balance of the wire represents the correct length of the pin. The skin-wire is now pushed up through the clips until its distal end is just below the lateral clip. Its pointed end will be out of the way over the lower part of the abdomen.

If the wire thus lying on the skin appears to be in suitable position, a guide wire parallel to it is drilled through the neck to the proper depth in the head. All that remains is to drive the Smith-Petersen nail over it. If the skin wire is slightly mis-

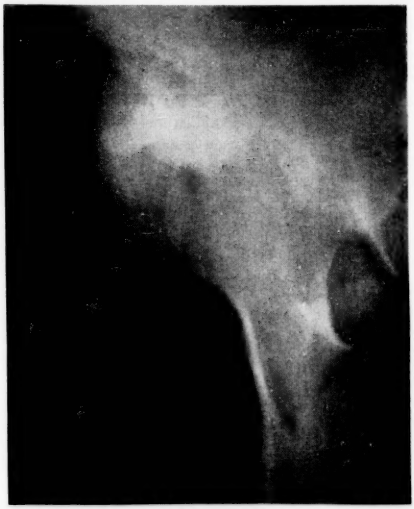


Fig. 2.—Lateral roentgenogram showing skin wire about 3/4 in. anterior to the femur and nearly parallel to the neck.

angled (in obese patients its proximal end will be angled anteriorly when it is pushed over the abdomen), the drilled wire can be inserted at the corrected angle. Thus, it is often possible to reach a suitable position with the first guide wire drilled. This technique has been used in 35 cases and has proved to be a rational, timesaving measure.

13 S. Goodman St. (7).

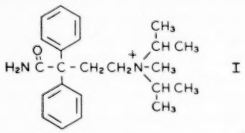
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Isopropamide Iodide.—(3-Carbamoyl-3,3-diphenylpropyl)diisopropylmethylammonium iodide.—The structural formula of isopropamide iodide may be represented as follows:



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Actions and Uses.—Isopropamide iodide, a synthetic anticholinergic compound, produces the peripheral effects of atropine and the belladonna alkaloids. Although it is chemically classified as a quaternary ammonium compound, the drug does not elicit sympathetic ganglionic blocking effects except at doses greatly in excess of therapeutic levels. Isopropamide differs from other anticholinergics chiefly with respect to duration of action. Since the drug apparently possesses an inherently prolonged action, antisecretory and spasmolytic effects can be maintained with the administration of single doses at intervals of 12 hours. It is useful as an adjunct to the management of peptic ulcer and other conditions of the gastrointestinal tract that are characterized by hypermotility and hyperacidity. Side-effects referable to therapy with isopropamide are those of anticholinergics in general and include dryness of the mouth, blurring of vision, and difficulty in urination. The drug is contraindicated in patients with glaucoma, prostatic hypertrophy, obstruction at the bladder neck, stenosing peptic ulcer, or pyloric or duodenal obstruction.

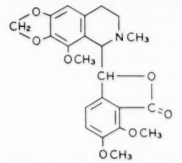
Dosage.—Isopropamide iodide is administered orally. Dosage should be adjusted to the needs of the individual patient as determined by clinical response and appearance of side-effects. The usual dose for adults is 5 mg. every 12 hours.

Preparations: tablets 5 mg.

Applicable commercial name: Darbid.

Smith, Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of isopropamide iodide.

Noscapine.—2-Methyl-8-methoxy-6,7-methylenedioxy-1-(6,7-dimethoxy-3-phthalidyl)-1,2,3,4-tetrahydroisoquinoline.—The structural formula of noscapine may be represented as follows:



Actions and Uses.—Noscapine is one of the isoquinoline alkaloids of opium. Except for morphine, it is the most abundant of the opium alkaloids, occurring to the extent of 6% in the seed capsules of Papaver somniferum. Because of its derivation from the opium poppy, the drug was formerly known as narcotine and was employed empirically in the past as an analgesic, hypnotic, and sedative. More recent evidence has shown that the drug bears little similarity, either chemically or pharmacologically, to morphine or the narcotic alkaloids of opium; hence, it has been renamed noscapine.

Noscapine shows papaverine-like effects on smooth muscle, causing coronary vasodilation in animals and, in large enough doses, bronchodilation. In man, there are no marked symptoms after administration of moderate doses. The drug produces none of the usual opiate-like effects such as constipation, miosis, blood pressure changes, and respiratory depression. Analgesia, hypnosis, and sedation are negligible or nil. Noscapine is rapidly absorbed from the gastrointestinal tract. Little is known about its metabolic fate or excretion.

The pharmacological action upon which the clinical use of noscapine is based resides in its ability to suppress the cough reflex in experimentally induced cough in animals and human volunteers and in patients with respiratory disease. The drug reduces the frequency and intensity of coughing paroxysms. Its antitussive potency under these experimental conditions is approximately equal, milligram for milligram, with that of codeine, both drugs having approximately the same onset and duration of action. In humans, clinical experience

with the drug in cough of pathological origin has not been sufficiently extensive to establish its final status.

Therapeutically effective doses of noscapine are essentially devoid of the unpleasant side-effects of codeine, and, except for occasional instances of nausea (which rarely proceed into vomiting), its side-effects are negligible. As with any antitussive agent, it should not be given in situations in which retention of respiratory secretions or exudates may be harmful.

Although noscapine is an opium alkaloid within the scope of the Harrison Act, it is exempt from requirements for order by prescription under certain conditions. However, experiments have shown that moderately large doses have no morphine-like effects in former addicts and no ameliorating effect on the severity of the morphine abstinence syndrome. Further, virtually no tolerance to the antitussive effect of the drug has been demonstrated. Hence noscapine is, for practical purposes, without addicting liability.

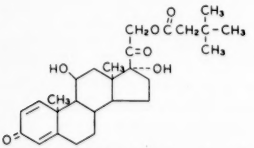
Dosage.—Noscapine is administered orally. The usual dose is 15 to 30 mg. given three or four times daily.

Preparations: powder (bulk).

Applicable commercial name: Nectadon.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of noscapine.

Prednisolone Butylacetate.—Prednisolone *tert*-butylacetate.—$\Delta^{1,4}$-Pregnadiene-3,20-dione-11β,17α,-21-triol *tert*-butylacetate.—The structural formula of prednisolone butylacetate may be represented as follows:



Actions and Uses.—Prednisolone butylacetate, a very slightly soluble ester of prednisolone, is suitable for intrasynovial and soft tissue injection. The drug appears to have a slightly greater potency and a longer duration of action than the acetate or butylacetate esters of hydrocortisone. It is useful for the treatment of those painful disorders of the joints, tendons, and bursae which are usually responsive to local glucocorticoid therapy (injection). Since the drug is so slightly soluble, 24 to 48 hours may elapse after injection before relief of symptoms becomes significant. The duration of relief varies from patient to patient but averages from two to three weeks. A continuation or even an increase in local discomfort (postinjection flare) may occur and be present for several hours after the administration of prednisolone butylacetate; however, this is usually followed by effective relief of pain and improvement in local function. Systemic steroid effects are not a problem when therapeutic doses are employed; with higher dosage, mild transient subjective improvement of joints remote from those injected has been reported. (See the general statement on glucocorticoids in New and Nonofficial Drugs.)

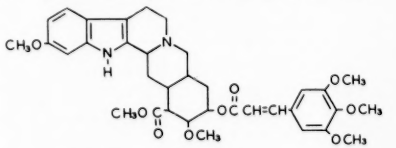
Dosage.—Prednisolone butylacetate is administered by intrasynovial or soft tissue injection only; it should not be given by any other route. The usual techniques governing intrasynovial (intra-articular and intrabursal) injection should be observed, and a 22-gauge or larger needle should be employed. The injection site may be infiltrated with a local anesthetic if necessary. Dosage and interval between injections depend on size of joint, degree of inflammation, and individual response of the patient. For large joints such as the knee, the usual dose is 20 to 30 mg.; in smaller joints, 7.5 to 10 mg. may be sufficient. A dose of 20 to 30 mg. is usually employed for the treatment of most forms of bursitis. The suggested dose for inflammatory conditions of the tendons is 4 to 10 mg. For the treatment of ganglion, 10 to 20 mg. is injected directly into the cyst cavity.

Preparations: suspension (injection) 20 mg. in 1 cc. and 100 mg. in 5 cc.

Applicable commercial name: Hydeltra-T.B.A.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of prednisolone butylacetate.

Rescinnamine.—3,4,5-Trimethoxycinnamic acid ester of methyl reserpate.—The structural formula of rescinnamine may be represented as follows:



Actions and Uses.—Rescinnamine, a purified ester alkaloid of the alseroxylon fraction of species of Rauwolfia, is closely related in chemical structure and pharmacological action to reserpine. Thus, rescinnamine is useful for the management of mild, labile hypertension and as a tranquilizing agent in agitated patients with simple neuroses and frank psychoses. While clinical experience with rescinnamine is not as extensive as that with reserpine, most observations indicate that both drugs are of approximately the same order of effectiveness.

Although all the side-effects and toxic reactions that occasionally follow the administration of reserpine have been reported after therapy with rescinnamine, the incidence and severity of some of these may be less with the latter agent. Sedation and

bradycardia, in particular, appear to occur less frequently and in milder form with rescinnamine. The incidence of other side-effects such as weakness and fatigue, nasal congestion, dizziness, confusion, increased appetite, and weight gain is about the same with both agents; in some patients, the severity of these effects may be slightly less with rescinnamine than with reserpine. Both drugs should be used with the same precautions, and both are subject to the same contraindications. (See the monograph on reserpine in New and Nonofficial Drugs.)

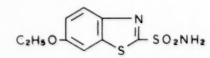
Dosage.—Rescinnamine is administered orally. For the treatment of mild hypertension or simple neuroses, initial doses of 0.5 mg. twice daily for two weeks have been employed. Thereafter, daily dosage requirements are either reduced or increased by increments of 0.25 mg., depending on therapeutic response and appearance of side-effects. While information available to date is not adequate to establish the dosage of rescinnamine for the treatment of institutionalized psychotic patients, daily amounts ranging from 3 to 12 mg. have been employed, apparently with satisfactory results.

Preparations: tablets 0.25 mg. and 0.5 mg.

Applicable commercial name: Moderil.

Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of rescinnamine.

Ethoxzolamide.—6-Ethoxy-2-benzothiazolesulfonamide.—The structural formula of ethoxzolamide may be represented as follows:



Actions and Uses.—Ethoxzolamide is a diuretic agent with actions and uses similar to those of the chemically related sulfonamide compound, acetazolamide. Both drugs are potent inhibitors of carbonic anhydrase and are believed to influence fluid mobilization by the same basic mechanism of action. Therapy with either results in alkalinization of the urine and a mild degree of metabolic acidosis. Available evidence indicates that the initiation of diuresis may be achieved with smaller doses of ethoxzolamide than of acetazolamide. On a weight basis, ethoxzolamide appears to be approximately twice as active as acetazolamide. Both have approximately the same duration of action, the effects lasting about 8 to 12 hours after a single oral dose.

Ethoxzolamide is used to produce diuresis in patients with mild to moderate congestive heart failure. It may also be used in conjunction with mercurial diuretic agents for the treatment of the more severe forms of heart failure. Such combination therapy may permit a reduction in the dosage and frequency of mercurial administration; in certain cases, it may even be possible to eliminate the need for the mercurial diuretic.

Ethoxzolamide decreases intraocular pressure by inhibiting the formation of aqueous humor. It is, therefore, useful in the treatment of glaucoma, particularly acute glaucoma. The drug is usually not employed alone but is given concomitantly with cholinergic miotics because such therapy appears to be additive. The long-term effectiveness of carbonic anhydrase inhibitors remains to be established.

Ethoxzolamide has been employed to reduce the incidence of convulsive attacks in epileptic patients subject to grand mal and petit mal seizures. Although beneficial effects have been reported in certain cases, there is insufficient evidence to establish the usefulness of the drug as an antiepileptic agent.

In general, ethoxzolamide appears to be well tolerated. The most commonly reported side-effects include nausea, dizziness, and numbness and paresthesias of the fingers and toes or at the mucocutaneous junctions of the lips or anus. Other less frequently reported reactions include drowsiness, fatigue, headache, and dryness of the mouth. Long-term therapy, such as is employed in chronic glaucoma, may lead to anorexia and weight loss. Side-effects generally subside or disappear with a reduction in dosage.

Ethoxzolamide should be used cautiously in patients with hepatic cirrhosis, since it may induce episodes of disorientation. The drug is contraindicated in patients with renal failure, hyperchloremic acidosis, Addison's disease, and in any condition in which sodium and/or potassium levels are depressed.

Dosage.—Ethoxzolamide is administered orally. For diuresis in mild to moderate congestive heart failure or in combination with mercurial diuretics in severe heart failure, a single dose of 62.5 to 125 mg. is given in the morning after breakfast for three consecutive days of each week; this dose may also be given on alternate days. In resistant cases, single doses of as much as 250 mg. may be required. For use in glaucoma, the dosage ranges from 62.5 to 250 mg. two to four times daily, depending upon the individual response in intraocular pressure. As is true for acetazolamide, the administration of ethoxzolamide should be intermittent rather than continuous. Dosage for the prophylaxis of epileptic seizures is not established, but daily amounts up to 750 mg. have been employed.

Preparations: tablets 125 mg.

Applicable commercial name: Cardrase.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of ethoxzolamide.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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PERINATAL MORTALITY AND MORBIDITY

DEATH is associated with birth and being born in the United States more often than it is with any disease except heart disease, cancer, and cerebral hemorrhage." With this Dr. Martha M. Eliot introduces her paper (see this issue, page 945), on Deaths Around Birth —The National Score. Accompanying Dr. Eliot's paper is one by Drs. Baumgartner and Pakter "assessing the local situation" and a third by Drs. Verhoestraete and Puffer presenting "a world view." The significance of the above quoted statement is attracting the attention of many in the medical and public health research field. Dr. Eliot expresses the tragedy involved in this loss of life as well as in the morbidity that too often accompanies child bearing and being born. The morbidity, or aftermath as it is sometimes called, is represented by the survival of infants with such conditions as cerebral palsy, epilepsy, mental retardation, and congenital malformations.

In assessing the local situation Drs. Baumgartner and Pakter recall the concerted attack on maternal mortality following a study made in 1933 and published by the New York Academy of Medicine. The report of that study indicated that two-thirds of the maternal deaths in New York City were then considered preventable. The effect was the establishment of city and county medical society committees to review and study all maternal deaths. By 1945 the maternal death rate was decreased to what was earlier thought to be the irreducible minimum. Ten years later, however, this "irreducible minimum" had been reduced by 70%. Although many other factors contributed to this dramatic reduction in maternal mortality, awareness of the problem and concerted efforts in its solution were certainly not the least. The authors show the relative lag in reducing infant mortality; this lag is especially evident when the early neonatal deaths (hebdomadal) are considered. In New York City the death rate during the first seven days after birth was 17.7 per 1,000 live births in 1955, compared to the relatively only slightly higher rate of 20.2 per 1,000 live births in 1937. Some of the factors responsible for this lag are suggested and some of the known remedial procedures are outlined. The need for more and better research on these problems is emphasized. A recent study indicating that many of these deaths of newborn infants are preventable has stimulated the formation of county and city perinatal mortality study committees and the organization within many hospitals of regular perinatal mortality conferences. Drs. Baumgartner and Pakter indicate that "much benefit is bound to accrue when the combined efforts and interest of the various groups are focused on a common aim of increasing knowledge concerning causes of death and preventing needless loss."

Presenting a world view, Drs. Verhoestraete and Puffer have observed that over a 40-year period the over-all infant death rate has declined rapidly in, for example, the United States, Sweden, and the Netherlands but that the decline in the neonatal and fetal death rates in these countries has been slower. In fact, the statistics indicate that within the early neonatal period in these years the death rate has remained almost constant. The importance of perinatal mortality (defined here as early neonatal and late fetal) as a major problem of wastage of life in technically developed countries is emphasized. The differences in perinatal mortality rates for countries of various stages of technical and socioeconomic development are outlined, as are many interesting relationships relative to causes of mortality in these countries. Drs. Verhoestraete and Puffer conclude that "an intensive program of research for the prevention of those conditions that determine the size of perinatal mortality rates appears, at present, necessary. The discovery of adequate preventive measures not only would allow further reduction of the perinatal problem in highly developed countries but might prove more generally applicable in technically less developed areas than programs of specialized care which are too costly and require too highly specialized skills and facilities to have any real effect within the low priority for program planning that can be given them at the present time."

These three articles serve well to point up the various aspects of and the many factors involved in the problems of perinatal mortality and morbidity. Because perinatal mortality and morbidity have been reduced remarkably in some areas of highly favorable circumstances in the United States and other countries as well, it is apparent that perinatal casualties could be reduced considerably if present knowledge of prevention were more widely and intensively applied. The necessity for more research is recognized, of course, in order that methods will be discovered for preventing deaths and morbidity from causes not now precisely known. Several questions concerning a concerted attack on the problems of perinatal mortality and morbidity are raised. Some of these are concerned with the need for more uniformity of terms and definitions; for more coordination of specialties and scientific disciplines in the clinical and public health approaches to study and research; for clarification and better recording of causes of death; for better pathological study; and for ways and means to reach those socioeconomic groups needing service but sometimes not seeking it and other times not knowing of its availability. And of especial interest is the emphasis that the above papers have placed on the morbidity aspects of conditions involving the perinatal period. This has been referred to as a "continuum of reproductive casualty."

958
167

It is with these problems and questions in mind that the Committee on Maternal and Child Care of the American Medical Association's Council on Medical Service is devoting its time and efforts. Through regional and other meetings, through research and study of present programs, and through publications, the committee is attempting to stimulate interest in and disseminate information on these problems of the perinatal period to the end that present knowledge will be utilized effectively. An example of this effort is the forthcoming series of articles to appear in THE JOURNAL entitled Study of Perinatal Mortality and Morbidity Programs in the United States. Simultaneously the committee is developing a Guide for Study of Perinatal Mortality and Morbidity that will be designed to assist state and county medical societies, state and local health departments, and community hospitals in their efforts to reduce deaths and the long-term illnesses resulting from conditions of the perinatal period.

CHANGING ASPECTS OF ENVIRONMENTAL HEALTH

There has always been change but in many fields the tempo of current changes has been greatly increased.[1] Environmental health measures were formerly concerned mostly with living micro-organisms and their living vectors. They must now include nonliving long-range stresses. The development of large metropolitan areas extending far beyond city boundaries has brought with it problems of coordinated control and cooperative effort. It is estimated that over 50% of the population in the United States now lives in such metropolitan areas. With this increase in urbanization more attention must be paid to air pollution, the conservation and treatment of water supplies, and the disposal of domestic and industrial wastes including the recent and ever-increasing problem of radioactive wastes. Noise and the increasing pace of life with mounting internal tensions and mounting accident rates, especially those connected with traffic, are also problems awaiting solution.

It has been said that human beings can adjust to any environment on earth, whether it be physical, chemical, microbial, or social, but this is true only within certain limits. In the past changes usually came about slowly enough to give man a chance to adjust gradually. Now that changes are occurring so fast it is becoming more and more evident that technological advances will have to be adapted to the capacity of the people to cope with the resultant environmental changes rather than that people will have to adjust to more rapid changes. Margins of safe tolerance will have to be determined.[2] This is an almost virgin area of research. Once determined, means of keeping environmental stresses within safe bounds must be found. The time is rapidly approaching when these problems must move beyond the conference stage. Concrete actions will have to be taken. Appropriate actions cannot be taken unless there is a greater public awareness of the nature, magnitude, and urgency of the problem. The cooperation of industry is necessary if we are to anticipate and prevent tragedies such as the fatal smog of 1948 in Donora, Pennsylvania, rather than to try to correct conditions after great damage has been done.

Speaking of the mental health aspects of rapid urbanization and the attendant problems already enumerated, Porterfield[2] points out modern man's need for more time for reflection and more chance for individual self-expression. The Brickdust Row of the near slums of O. Henry's time has been replaced by the prefabricated housing developments found in many modern suburbs, but the effect is the same. An atmosphere of monotony and regimentation is created and with it an aftermath of emotional frustrations and psychosomatic complaints in adults and delinquent behavior in youth. The environment must express not repress the individual.

1. Hollis, M. D.: Environmental Health Aspects of Future Metropolitan Area Complexes, Am. J. Pub. Health **48**:484-488 (April) 1958.

2. Porterfield, J. D.: Mental Health in the Environment of the Metropolitan Area of the Future, Am. J. Pub. Health **48**:489-494 (April) 1958.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Recently, leafing through an anthology of famous speeches, I lingered over Patrick Henry's deathless words on American liberty. I was struck by the realization that the evils against which he inveighed and the objectives which he so vehemently urged are substantially the same as those which confront us today. The choice which he was called upon to make challenges us today. In his ringing words, "The question before the House is one of awful moment to this country. For my part I consider it as nothing less than a question of freedom or slavery."

In their day, our forefathers strove to wrest their freedom from an alien government which, in defiance of the will of the people, sought to restrict and usurp the rights of the individual for the exaltation of the power of the few who typified the state. In our day, we are called upon to preserve that freedom against a threat which arises out of the tyranny of our own despotic selfishness.

If we proceed upon the misleading but appealing assumption that democracy is a system under which whatever the majority wants is good and whatever is good we are all entitled to have, then the road to national ruin will be paved by the indulgence of ill-considered and selfish desires.

Democracy is the most exacting and difficult of all systems of government because it demands of all citizens intelligence, integrity, and unselfish devotion. It asks most of us to be better than we are, but not better than we could be. It invites the lowliest to aspire to greatness, because no man can become great who does not serve a cause or an ideal more important than himself.

President Eisenhower sounded a note of warning for us all in his last address on the State of the Union. He declared: "Freedom has been defined as the opportunity for self-discipline. Should we persistently fail to discipline ourselves, eventually there will be increasing pressure on government to redress that failure. By that process freedom will step by step disappear."

That is why the members of the medical profession—alarmed more as thinking citizens than as physicians—look with suspicion and fear upon legislation which, in utter disregard of economic facts, promises nebulous mass benefits at the cost of essential, individual dignity and freedom. That is why we of the medical profession favor the utilization of voluntary means for the solvent individual citizen to defray the costs of the services and benefits which he chooses to enjoy.

We are convinced that programs which involve more and more taxation to pay for benefits made impartially available to all persons—in disregard of their individual need of such benefits or of their ability to provide them for themselves—are a threat to the character and freedom of our nation.

The end-result of such programs, we believe, will inevitably be the exaltation and expansion of the powers and rights of the state and the diminution and ultimate usurpation of the powers and rights of the individual citizens.

We physicians contend that it is the right and the duty of the individual American citizen, so far as he is able, to provide for himself and his dependents. We contend that his earnings should not be so drained off in soaring taxes as to make him no longer independent and self-sustaining. We contend that any program—at any level—which tends to do this is not only destructive of the character and status of the citizen as a free man but destructive of the character of our government.

This I believe and this I will defend as one who has had the distinct honor and privilege of serving as the one hundred eleventh President of the American Medical Association.

David B. Allman, M.D.
Atlantic City, N. J.

ORGANIZATION SECTION

STATEMENT REGARDING FHA-INSURED LOANS BEFORE A SENATE SUBCOMMITTEE BY R. B. ROBINS, M.D.

May 21, 1958

Mr. Chairman and Members of the Subcommittee:

I am Dr. R. B. Robins, a practicing physician of Camden, Arkansas. I am testifying today at the request of the chairman of the board of trustees of the American Medical Association, and I am pleased to give you the views of the American doctors on some of the problems of caring for our aged citizens. I am a past vice-president of the A. M. A. and past president of the American Academy of General Practice.

My testimony today will be concerned with the medical problems that are peculiar to the aged, the facilities available to care for their ordinary housing needs as well as their medical needs, the cost of these services, and the role of the proprietary nursing home in helping to solve some of these problems.

It is our understanding that the Federal Housing Administration presently is offering mortgage insurance for construction of large nonprofit institutional-type homes for the aged which may have a section for those needing nursing care.

My remarks today will be directed solely toward pointing out the need for a similar program of loan guarantees for proprietary as well as nonprofit organizations. I want to point out that currently 71% of nursing home patients are cared for in proprietary institutions.

As the basis for my testimony, I want to state that the American Medical Association, through its Board of Trustees, has approved and will support a government-insured loan program of the FHA type for nongovernmental hospitals and nursing homes whether their ownership is of a nonprofit or a proprietary character.

In recent years, the problems of the elderly have attracted an ever-increasing amount of national attention, both within the government and among groups and associations outside government. This is understandable since the proportion of our population over age 65 is increasing at a rate that might be described as amazing. In 1900 there were only 3,000,000 of these elderly citizens. Now there are approximately 15,000,000. Already they represent nearly nine per cent of our entire population, and the trend has not yet leveled off.

Not one but many factors explain how mankind has been extending its life span—advances in medical science, a new awareness of the principles of nutrition, better working conditions that allow more men and women to reach retirement age and better housing. All of these factors and others have contributed to the increased longevity of our population.

New problems naturally attend such gains, many of which can only be solved by persons skilled in furnishing medical care and nursing services.

From its beginning more than a century ago the American Medical Association has been deeply involved in medical aspects of caring for the aged. At work now in this field are three active committees attached to the Association's Council on Medical Service. They are the Committee on Aging, the Committee on Indigent Care and the Committee on Medical and Related Facilities.

Our work in these fields has been performed in cooperation with other interested agencies. In 1946, representatives of the A. M. A. met with representatives of the American Hospital Association, American Public Health Association, and the American Public Welfare Association, to establish the Interim Committee on Chronic Illness which, in May, 1949, was changed to The Commission on Chronic Illness, with representatives of the general public, industry, labor, agriculture, education, religion, social sciences, journalism, health, and welfare.

A number of studies were made. One of these I will leave with you, entitled "Nursing Homes, Their Patients, and Their Care," published by the U. S. Public Health Service which cooperated in this study.

Although the Commission was disbanded as such in June, 1956, the cooperating organizations continue to work on the parts of the program in which they are best qualified. The Council on Medical Service of the American Medical Association still prints the Newsletter on Chronic Illness, a copy of which is attached.

This interest of the A. M. A. continues right down the line to the family physician who is on the scene when the various medical crises occur in the lives of older people. A majority of our constituent state medical societies have formed committees on aging and are making their contributions. In addition, as a recent development, a series of regional meetings, sponsored by the A. M. A., has been held to stimulate local action in bringing the best possible medical care to senior citizens in their homes, in physicians' offices, in nursing homes and in hospitals.

I would like to mention several other concrete achievements that are the result of cooperative undertakings of the medical profession, the hospital and nursing home people, the insurance industry and the drug industry.

First, new treatment and surgical procedures have been developed to ease the discomforts of the ill and disabled aged, and in many cases to rehabilitate them to the point where they can take care of themselves and often return to employment. Some examples of this are cortisone, antibiotics, tranquilizers, early ambulation of operative cases, physical and occupational therapy, early evaluation of seriously ill and injured for vocational guidance and training.

Second, enrollment of older people under voluntary health insurance has increased at an encouraging rate in recent years. It has gone up about 100 per cent in the last seven years alone. Presently, exclusive of the approximately 3,000,000 older persons who receive public assistance, more than 50 per cent of those over 65 have some form of health insurance.

Third, the American Medical Association has joined with the American Hospital Association, the American Dental Association and the American Nursing Home Association in the formation of the Joint Council to Improve the Health Care of the Aged. The council's long-range goal is better health for all the aged. Its most immediate concern is working out answers to meet the financial and social problems that accompany chronic illness.

Fourth, hospitals are actively experimenting with gradations of care, a new concept that attempts to fit the patient to the type of care he needs, but not for complete hospital care when that is not required.

Fifth, for the last year, representatives of the American Medical Association and the American Nursing Home Association have been meeting regularly to prepare improved medical care standards for the nursing homes, standards that admittedly are badly needed in some sections of the country.

In February of this year the first national conference on nursing homes and homes for the aged was held here in Washington. I offer for the record a summary of that conference's report, containing information supporting our request for action in this field.

Most of the aged ill or disabled can, and are, best cared for in the physician's office or in their homes, still others require care in a medical facility. The question is, do these people need care in a general hospital at a cost of $20 to $25 per day? Some of them do, but others could receive the maximum professional attention their condition calls for in a less expensive facility—a properly constructed and operated nursing home, with professional medical and nursing care at hand or readily available. I am speaking now of older people with conditions that are chronic, such as . . . hypertension, diabetes, arthritis, paralysis of extremities.

There is a much larger group who require some nursing and medical care, and who could be provided for quite satisfactorily in private homes. Yet, for many reasons, the relatives—if there are relatives—are not in a position to take in these older people. They need housing, and some medical care, but not hospital care in many cases. Yet, many thousands of them are in hospitals, merely because there are not suitable nursing homes or other chronic disease facilities.

This situation points up the critical need for new and improved facilities tailored to the specific health requirements of the older citizens. Nursing home administrators have appeared before your committee earlier. They have convincing evidence, accumulated over recent years, that they can not provide the services they want to provide in quality or in quantity because they are unable to obtain the credit they need on reasonable terms.

The normal lending agencies just are not making loans to proprietary nursing homes in any significant volume. The lenders have their reasons—because the homes generally are one-purpose structures, unattractive as a straight commercial risk, even though foreclosures are rare.

As doctors we know the need for attractive, clean, safe nursing homes, where we can be sure our older patients will receive the proper nursing care under our direction, and where the costs will not be prohibitive.

Through Hill-Burton and other programs the federal government for years has been assisting public and nonprofit hospitals through money grants. The proprietary nursing homes are not asking grants, but only a federal guarantee to make it possible for them to obtain the mortgages they need. They will pay the going rate of interest including the mortgage insurance premium and will repay the loans.

We strongly urge this committee to consider an insured type loan for which proprietary and nonprofit nursing homes could qualify, under FHA. This would stimulate the local lending agencies and bring about an atmosphere that would produce the capital needed for construction and equipment.

I do not know of a single group in the medical field that does not now urge the construction of special facilities for the chronically ill and for the aged. That is exactly what a well-equipped, well-administered nursing home is. All medical authorities with whom I have been in contact believe this to be one of the really critical medical shortages today.

LETTER REGARDING POSITION OF ASSISTANT SECRETARY OF DEFENSE

May 13, 1958

Honorable Carl Vinson
Chairman, Armed Services Committee
House of Representatives
Washington 25, D. C.

Dear Mr. Vinson:

The American Medical Association has been following with a great deal of interest the public hearings currently being conducted by the Armed Services Committee of the House of Representatives relative to the reorganization of the Department of Defense.

The Association has demonstrated for more than a century its sustained interest in seeing that the best available medical services are provided for our Armed Forces in time of war or peace. In recent years, since the enactment of the National Security Act of 1947, the Association has been instrumental in presenting, to both the legislative and executive branches of government, the need for health and medical policy coordination at the highest level of our government. The first Hoover Commission in 1948 recommended that strong control over military medical policy be exercised from the level of the Secretary of Defense.

In July, 1949 the position of Assistant to the Secretary of Defense for Health and Medical Affairs was established, and in 1953 this position was changed to that of Assistant Secretary of Defense (Health and Medical). Through the operations of this office and with the cooperation of the Surgeons General of the various branches of the Armed Forces an enviable record of increased efficiency and economy has been established.

Since the establishment of this position the military medical services have experienced the lowest case fatality rates of any military service in peace or wartime. At the same time, the military medical services have maintained the highest effective rate of any military service, even though in many instances American Armed Forces were serving in disease ridden areas throughout the world and under the most hazardous conditions of peacetime and wartime. Furthermore, the military medical services established the first unified supply procurement agency of the Armed Forces, which with a Department of Defense blood program, reaching to our world-wide military outposts, proved highly efficient during the Korean campaign.

Joint utilization of military medical facilities, educational programs, military logistics, including patient evacuation, intelligence and operations, and research and scientific developments have also been made possible under the directorship of the civilian Assistant Secretary of Defense (Health and Medical) and his predecessors. The interservice use of military medical facilities, including hospitals and dispensaries, as well as the interservice staffing of military hospitals has been accomplished by programs directed from this office.

During the Korean Conflict, this office of the Department of Defense directed the coordination of medical and health liaison with the Forces of the United Nations, and this has been continued with the NATO and SEATO Forces. During this same period, this office established the first interagency medical council, responsible for the coordination of the federal medical effort on behalf of our wartime and peacetime missions of health and medical care.

Experience has clearly shown that as a result of the respect and authority vested in an Assistant Secretary of Defense it is possible for him to formulate policy and direct the programs of the military medical services of the Department of Defense, while at the same time commanding the respect of his opposite numbers in the highest circles of our own government, in foreign governments and in the professional and scientific as well as lay national and international groups.

We know that the prestige of the military medical services has increased since establishment of this office both in this country and abroad, particularly in the eyes of civilian medicine.

In summation, we believe, therefore, that it is in the best interests of the Armed Forces, the military medical services, and our country that the position of Assistant Secretary of Defense for Health and Medical Affairs be maintained in the Department of Defense organization with a civilian physician appointed to this position.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

A. M. A. LEGAL CONFERENCE FOR MEDICAL SOCIETY REPRESENTATIVES

A panel discussion on the legal aspects of medical practice through "third party" mechanisms involving some hospitals, closed panels, medical schools, and management and union health plans occupied a full day's session in Chicago, in May, for 150 medical society representatives. It was the second legal conference to be sponsored by the Law Department of the American Medical Association—attracting executive secretaries, attorneys, and consultants from 35 states and the District of Columbia.

Discussing the medical care program of the United Mine Workers of America welfare fund, Arthur H. Clephane, legal counsel for the Medical Society of the State of Pennsylvania, said: "The

profession everywhere must sit down with the U. M. W. A. and with all leading third parties across the conference table as men of good will and develop a plan for working together which will insure the best quality of medical care to the third party beneficiaries which is reasonable and fair to the funds and to the doctors."

John Lansdale Jr., legal counsel for the Cleveland Academy of Medicine, speaking on "Hospitals and the Practice of Medicine," said: "Medical practice is basically medical judgment, and not the technique or effort specifically or in itself." Francis Shackelford, special counsel for the Medical Association of Georgia, reported details of a recent cooperative agreement reached by organized medicine in Georgia with the University of Georgia School of Medicine, relating to faculty treatment of fee-paying patients at the university's Talmadge Memorial Hospital. After a special committee of officials from the A. M. A. and the Association of American Medical Colleges visited the school to resolve differences, a spokesman said: "It may well be that this committee has established a precedent which may prove quite beneficial in the resolution of similar situations."

Legal aspects of membership in county medical societies were discussed by Eugene R. Warren, counsel for the Arkansas Medical Society. The panel moderator, A. Leslie Hodson, a Chicago attorney who acts as an A. M. A. consultant, commented: "Extreme care should be taken by local societies in rejecting applications for membership or disciplining an existing member simply and solely because he is a member of a closed panel." Charles Margett, legal counsel for the Medical Society of Queens, reported on "Closed Panel Types of Practice."

Other Program Topics

On May 10, the second day of panel sessions, Edwin J. Holman, of the A. M. A. Law Department, related results of a national survey on professional liability; Jule M. Hannaford, counsel for the Minnesota State Medical Association, discussed "Hospital Records and Tissue Committees," and Jake Hunt, counsel for the Oklahoma State Medical Association, reviewed "Group Programs and Professional Liability Insurance Review Committees." Attorney Don H. Reuben of Chicago discussed libel, slander, and privacy in medicine, A. M. A. Attorney Bernard D. Hirsh reported on "Tax Advantages of Corporations and Unincorporated Associations," and Robert Throckmorton, counsel for the Iowa State Medical Society, spoke on legislation and lobbying practices of state medical societies.

Welcoming and introductory comments were delivered to the conference by A. M. A. President David B. Allman, A. M. A. General Manager F. J. L. Blasingame, and C. Joseph Stetler, director of the A. M. A. Law Department. Those attending received first-issue copies of a new A. M. A. monthly news letter, *Citation*, which highlights the latest important court decisions or other legal developments affecting medicine.

SCIENCE FAIR WINNERS TO EXHIBIT IN SAN FRANCISCO

Two teen-age scientists, winners of the A. M. A. top honors at the National Science Fair in Flint, Mich., May 7-10, will be guest exhibitors of the Association at its Annual Meeting in San Francisco, June, 23-27.

For the third consecutive year, the A. M. A. participated in the fair by selecting four exhibits in the basic medical sciences. The two first place winners are Clare L. Chatland, aged 16, a junior in Missoula County High School, Missoula, Mont., and David R. Brown, aged 15, a St. Louis Park

Congratulating the winners, Clare L. Chatland and David R. Brown, who will exhibit their work at the A. M. A. Annual Meeting in San Francisco, are, *left*, Dr. Otto J. Preston, chairman, National Science Fair executive committee, and, *right*, Dr. Thomas G. Hull, Chicago, Secretary, A. M. A. Council on Scientific Assembly, who served as a judge.

High School sophomore in Minneapolis. Clare's exhibit on "Hypersensitivity" shows the results of an experiment with the permeability of sensitized and nonsensitized membranes of mice. David's exhibit on "Humeral Transplants" shows how fetal mouse bones become ossified when transplanted into hostile mediums. Honorable mention citations were awarded to Barbara Ann Conway, aged 16, Chattanooga, Tenn., for her work with "Experimental Teratology," and to Robert LeRoy Sayre, aged 17, Huntington, W. Va., for his demonstration of "The Neurohumeral Theory and Cardiac Inhibition."

Dr. Alphonse McMahon, Chairman, A. M. A. Council on Scientific Assembly, and fellow Council members Drs. Stanley P. Reimann, Philadelphia,

Henry R. Viets, Boston, and Thomas G. Hull, Chicago, chose the exhibits from a field of 281 entries from 41 states, the District of Columbia, Alaska, Hawaii, Germany, and Japan.

The awards were presented at an A. M. A. luncheon attended by 820 students, teachers, regional fair sponsors, press, and medical representatives. Dr. George W. Slagle, president, Michigan State Medical Society, presided over the presentations, and Dr. Otto J. Preston, chairman of the fair's executive committee and immediate past-president of the Genesee County Medical Society, Flint, announced the awards.

Many of the participating 146 regional fairs are co-sponsored and supported by local state and county medical societies, and the A. M. A. awards at the National Science Fair are the annual highlight of the medical profession's efforts to encourage talented students to undertake a medical career. The 1959 National Science Fair will be held May 6-9 in Hartford, Conn., and in Indianapolis, in 1960.

958
167

LETTER REGARDING FEDERAL CIVIL DEFENSE FUNCTIONS

May 13, 1958

Honorable Chet Holifield
Chairman, Military Operations Subcommittee
Committee on Government Operations
U. S. House of Representatives
Washington 25, D. C.

Dear Mr. Holifield:

The American Medical Association is advised that the President's Reorganization Plan No. 1 of 1958, providing new assignments for the conduct of federal defense mobilization and civil defense functions, is currently being considered by the Military Operations Subcommittee.

As the Association understands the proposed plan, its purpose is to enhance and make more effective the role of the Federal Government in nonmilitary defense programs. Under the Plan, the broad program responsibilities for coordinating and conducting the interrelated defense mobilization and civil defense functions would be vested in the President for appropriate delegation. The Office of Defense Mobilization and the Federal Civil Defense Administration would be consolidated in a new agency which would be known as the Office of Defense and Civilian Mobilization.

The basic concept of national mobilization is accepted as the "will of the people to resist." This concept depends on the sustained physical and mental health of the people and as such has interested the American Medical Association for many years.

In its concern with the health and medical aspects of civil defense, the Association has recognized, for a number of years, the urgent need for federal leadership, direction, and coordination. The Association believes that civil defense, like military defense, is an integral part of national defense which requires greater federal responsibility and leadership.

More specifically, the Association is concerned with the status, in any federal agency, of the office responsible for medical and health activities. The Association is convinced that medical and health activities are one of the most, if not the most, important function in sustaining the "will of the people to resist." In June, 1954, the Association's House of Delegates adopted a resolution requesting the Administrator of the Federal Civil Defense Administration to re-examine the position of the Health Division and to elevate that Division to a status commensurate with its obligations and responsibilities. In principle, this was ultimately accomplished in the December, 1957, reorganization of the Federal Civil Defense Administration with the creation of the position of Assistant Administrator, Health and Medical Affairs.

In June, 1956 the Association's House of Delegates approved the broad objective of strengthening the federal civil defense program, but was of the opinion that the method of accomplishing this was a matter for determination by the Congress with the advice and assistance of the President and the state governments.

In testimony before your subcommittee on March 7, 1957 on H. R. 2125, 85th Congress, the Association again emphasized that the medical and health functions of the civil defense program merit stature and prestige commensurate with the duties and responsibilities which must be assumed. Within the organization of the Office of Defense Mobilization there now is established a position of Assistant Director for Health and a civilian Health Resources Advisory Committee. The Association believes that the health and medical functions of the Federal Civil Defense Administration and the Office of Defense Mobilization must be maintained at top level in the organization of the proposed Office of Defense and Civilian Mobilization for the good of our country and our people should our nation ever again be confronted with another national emergency.

The Association is confident that the subcommittee, in furtherance of its serious efforts to strengthen the civil defense and mobilization program of our

country, will give this matter of medical and health affairs the urgent and earnest attention which it merits.

We would appreciate it if you would make this letter a part of your official record of the hearings.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

TEACHING OF FORENSIC MEDICINE

The A. M. A. Committee on Medicolegal Problems, headed by Dr. Alan R. Moritz of Cleveland, is studying some suggested subjects in the field of forensic medicine for consideration and possible inclusion in medical school curriculums. Although the topic is integrated with other subjects in many medical schools, a number of schools now do not formally include forensic medicine in their instructional programs. Plans call for submitting an initial draft of the Committee's report to the Council on Medical Education and Hospitals for review and comment.

AMEF LISTS DIRECT ALUMNI SUPPORT TO MEDICAL SCHOOLS

A total of 50,364 alumni donated $3,020,600 directly to the 85 medical schools in the United States last year, according to a report of the American Medical Education Foundation, which handled an additional $984,884 in donations. Nearly half of the direct contributions, $1,467,098, were made without restriction, while the remainder were designated for building funds, research, student aid, library, endowment, and other earmarked uses.

California led the nation in total contributions, $652,883, through combined AMEF and alumni efforts, and the state was also in first place in total gifts, 19,482—including a top-ranking number of 14,685 donations through the foundation. Direct appeals brought $487,778 to California medical schools, more than to schools in any other state making such campaigns.

By individual school, the alumni of Jefferson Medical College in Pennsylvania led in number of direct contributors, 3,746. As the result of a special building fund campaign, alumni of the University of Vermont College of Medicine contributed the largest direct amount to a single medical school, $226,752. Other schools receiving large amounts in direct contributions through alumni drives (all more than $115,000) were Stanford University School of Medicine, University of Arkansas School of Medicine, College of Medical Evangelists, Harvard Medical School, Tulane University School of Medicine, New York University College of Medicine, Johns Hopkins University School of Medicine, and the University of Pennsylvania School of Medicine.

ACCREDITATION IN INDUSTRY

Representatives of the A. M. A. Council on Industrial Health and Council on Medical Education and Hospitals have joined with spokesmen for the Industrial Medical Association and the Joint Commission on Accreditation of Hospitals in discussions as to the possibility of developing a system for jointly accrediting occupational medicine services in industry. The first meeting was held in Chicago on May 15, and recommendations were sent soon afterwards to the respective parent-groups for action.

LIAISON WITH SCIENCE WRITERS

A cooperative effort to develop better liaison of the medical profession with newspaper science reporters has been launched by the A. M. A. and the National Association of Science Writers. The first of a series of regional workshops was held in Syracuse, N. Y., in April, for 70 participants from northeastern United States. Cincinnati was the scene of a second conference May 22. Present plans call for continuing the sessions—primarily panel discussions—in other parts of the country next fall.

Serving as co-chairmen of the Syracuse meeting were Dr. Robert J. Collins, president of the Onondaga County Medical Society, and Mrs. Cathy Covert of the Syracuse *Herald-Journal*. At a luncheon session, the first public report of Hungarian health under Communist rule was delivered by Dr. Lawrence H. Hinkle Jr., associate professor of clinical medicine at Cornell University Medical College. He said: "The Communists do not possess methods of persuasion, teaching or indoctrination that are superior to our own. This should go a long way toward dispelling the myth of so-called 'brain washing.'" Topics discussed at panel sessions included defining a good science story, a reporter's source file, how to use medical news sources, and ethics.

A similar pattern of panel discussions was used at the Cincinnati meeting. One highlight of that workshop was a report by Bernard C. Wexler, Ph.D., of Cincinnati on "Accelerated Aging in the Salmon and Its Application to Man." His study was made in collaboration with Dr. O. H. Robertson, emeritus professor of medicine at the University of Chicago School of Medicine. Dr. J. Robert Hudson of Cincinnati, and Don Dunham, science writer for the Cleveland *Press*, served as co-chairmen.

The National Association of Science Writers was founded in 1934. Its membership of 300 is confined to reporters who specialize in the writing of medical and science news.

HEALTH MESSAGES ON RADIO

The latest report of the Bureau of Health Education shows that 574 sets of A. M. A. transcriptions were in the hands of local broadcasters throughout the country as of April 28, 1958. Since there are 13 programs in each set, this represents about 7,500 local broadcasts which have been made, are being made, or will be made from these transcriptions. Some of the most popular series include "Menu for Health," 45 sets; "Harmony and Health," 46 sets; and "Interlude," 28 sets. Not included in these figures are the monthly platters entitled, "Health Magazine of the Air."

GRAND ROUNDS AT THE SAN FRANCISCO MEETING

The seventh in the series of Upjohn Grand Rounds telecasts will originate in San Francisco on June 25th, 1958 (6-7:30 p.m. Pacific daylight-saving time). This Grand Rounds will be the first of the series produced in cooperation with the American Medical Association and will be a part of the regular annual meeting. The program will be transmitted via closed circuit television to eight cities: Boston, Chicago, Cleveland, Kalamazoo, Mich., New York, Philadelphia, and Syracuse, N. Y. Physicians attending the meeting will have an opportunity to view the program in the War Memorial Opera House, one block from the Civic Auditorium.

The program will be in two segments. The first half-hour will be devoted to "Highlights of the Annual American Medical Association Meeting." Specially newsworthy scientific exhibits will be presented and the physician responsible for each of the exhibits will be interviewed. In addition, this segment of the program will present excerpts from some of the significant clinical papers that will be heard by those gathered in San Francisco. The second segment of the program will originate from the newly completed amphitheater of the University of California Medical Center. The subject to be discussed by a panel of outstanding physicians in the field of diabetes will be "The Current Therapy of Diabetes."

Case presentations of the patients from the wards and the outpatient clinics of the University of California School of Medicine will precipitate discussion of the recent developments in diabetes therapy, including the judicious utilization of the oral hypoglycemic therapy. The panel will also consider the question of shifting appropriate patients from insulin to oral tolbutamide therapy and delineate the proper steps and precautions in such a situation.

As usual, the entire program will be recorded on kinescope film and will subsequently be available for 16-mm. motion picture presentation to county medical societies and other professional medical groups.

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

COUNCIL ON MEDICAL SERVICE

CONFERENCE OF BLUE SHIELD PLANS

"Blue Shield's most significant problems lie in physician relations, national enrollment, federal legislation, and the development of more progressive forms of Blue Shield coverage."

Dr. A. J. Offerman, Omaha, retiring president, thus keynoted the 1958 Conference of Blue Shield Plans. The conference, held in Chicago the last week in April, was attended by approximately 700 persons.

In accepting Dr. Offerman's charge, the conference adopted a resolution in opposition to the Forand bill and revised its bylaws and membership standards. Other actions and discussions gave high priority to enrollment expansion, the effects of relative value studies on the plans, and the role of the physician in Blue Shield's future.

Dr. Carlton E. Wertz, Buffalo, was installed as President. Dr. Frank L. Feierabend, Kansas City, and Dr. M. Shelby Jared, Seattle, were named President-elect and Vice-president respectively. New officers of the Blue Shield Board of Directors (formerly Blue Shield Commission) include Dr. Donald Stubbs, Washington, D. C., Chairman; Dr. Henry Blake, Topeka, Vice-chairman, and Dr. Dwight Needham, Syracuse, N. Y., who was reelected as Secretary.

The conference's resolution opposing the Forand bill pointed out that of the 42 million Blue Shield subscribers "approximately 6.5% are in the age group of 65 years or over as compared with 8.5% of the total United States population 65 years and over."

Dr. Louis H. Bauer, Board Chairman of United Medical Service, Inc. of New York and Secretary-General of the World Medical Association, spoke on how plan trustees can best serve the future of Blue Shield.

In his address, Dr. Bauer said, "Some of our plans are no longer doctors' plans except in name. Not all of this is Blue Shield's fault, but often it is the fault of the medical society in letting control of the plan slip out of its hands. The fact remains, however, that, whatever the reason, it is the duty of the Board of Trustees to see to it that this control is strengthened or, where necessary, returned to where it belongs—in the hands of the profession. The key to the correct balance of Blue Shield strength lies in the relationship of the board to the medical societies it represents. . . .

"The medical societies should have the right to nominate the medical members of the Blue Shield Board. Ideally, in small plans, they can perhaps elect them. But no physician trustee should be elected unless he has been at least nominated or approved by the medical society of which he is a member.

"Plan trustees must see to it that no major change in policy is approved by the board unless the changes first meet with the approval of the medical societies. This applies to such plan policies as the extent of coverage offered, service benefit levels, fee schedules, and so forth."

Commenting on the relationship of Blue Shield to Blue Cross, Dr. Bauer said, "There was a tendency in the early years, because Blue Cross was the older, more experienced partner, for Blue Cross to become the dominant half of the liaison. Now, however, the situation is changed. Blue Shield has a depth of experience it lacked before and is growing faster than Blue Cross. I believe the two plans should now be partners on an equal footing. Neither should dominate the other.

"If we look at the plans around the country we see some of them completely divorced from one another. Others are almost completely unified, even to having the same personnel on both boards. Still other plans are separate except for a joint enrollment department. This, especially in the larger plans, has often proved a great convenience and saving to both plan and subscribers.

"Complete integration, even of just the boards, however, does not seem to me to be in the interest of anyone. Blue Cross is controlled by the hospitals and Blue Shield by the physicians—and their philosophies differ in so many respects that it is hard to imagine any joint board working smoothly without one plan overpowering the other.

"It is very disheartening to view the state of affairs that exists in those areas where the two organizations are more or less one in fact, even if not in theory. Because Blue Shield has been the junior partner it seems often to act hesitantly, without vigorous conviction in the course it must follow, content to be hand-led and spoon-fed by the elder Blue Cross. What is to be gained by one plan hiding in the shadow of the other? Blue Shield is no longer in swaddling clothes. It has reached adult state. Both plans are working to serve the community. They should work in harmony, yes—share those duties that will benefit both plans—but each plan should be master of its own fate.

"The first step that should be taken to establish a Blue Shield plan's independence is the appointing of a director separate from Blue Cross. Certainly, when Blue Shield was in its infancy, it could not afford a full-time director. Since there was need to establish a good deal of early planning, much was gained by having Blue Cross' director also serve Blue Shield. But, again, things have changed—and just as there is much to be gained by having separate boards, so is there much to be gained by each plan having its own director. The duties and responsibilities of each plan have grown to too great a height to allow one man to fulfill both jobs effectively without one being secondary to the other."

Dr. Offerman, in his presidential report, commented on the need for redoubling efforts to establish effective avenues of communication among all physicians and to create more opportunities for members of the profession to participate individually in the affairs of Blue Shield.

Also, Dr. Offerman said, "We must immediately devise better and more effective means of reaching the younger men entering the practice of medicine so that each new generation of physicians will be equipped to play a proper role in the development of our plans. The medical profession alone can provide the guidance and leadership essential to our progress. And this leadership can only be stimulated and assured if physicians understand the fundamental concept of physician sponsorship and guidance behind the growth and development of our community plans. For months—even years—we have told ourselves and agreed among ourselves that professional relations is the lifeblood of Blue Shield. It is time we demonstrate this tangibly with bold programs of action calculated to generate active physician participation in all the affairs of Blue Shield."

Elaborating on this theme, Dr. Ira C. Layton, Kansas City, in his address entitled "Charting a Course for Progress in Blue Shield," said, "I am convinced that the successful professional relations program can be carried out only by word of mouth from doctor to doctor.

"This necessitates a program of intensive training of a few physicians through the medium of board and committee activity so that facts may be carried to hospital coffee rooms and lounges, where they will be heard by other members of the profession. It necessitates our risking turnover of mem-

bership on our boards of trustees and on important committees, so that additional physicians may become better trained and better understand Blue Shield problems. Admittedly, this involves some risk; but without it, I fear we cannot succeed. In the broad sense, much can be done to improve professional relations by returning to the profession and to sponsoring medical societies the prerogatives of nomination and election of board members and by offering to the specialty societies the privilege of selecting members for important committees, such as fee schedule committees, arbitration committees, and others."

Both Dr. Offerman and the enrollment committee's report discussed progress in enrollment of national groups.

Dr. Offerman commented, "Out of the diversity of local Blue Shield programs traditionally aimed at meeting purely local needs and conditions, a pattern of benefits approaching the needs of national employers has been evolved. No one pretends that we have achieved the ultimate in our efforts to develop an entirely suitable national 'product.' It is, however, significant that we have made important strides in that direction. We have much more to do. Competition for enrollment among important national accounts is becoming more intense, and to meet it with success we will have to prepare Blue Shield to compete as favorably as possible for this business. Therefore, it is essential that we all contribute our best thinking in moving ahead toward a progressively better program of coverage for national employers. I would urge that this be an objective of first priority for each plan."

The enrollment committee reported that 39 plans agreed to underwrite the benefits of the national account agreement. These plans represent over 68% of the entire Blue Shield enrollment. A national group contract has been prepared, and Medical Indemnity of America, the central contracting agency, is now in the process of filing it with the New York State Department of Insurance. The committee emphasized the necessity for "a united front to the national market so that the name Blue Shield on a national contract will mean the same thing in all cases."

This committee also called for balanced benefits between Blue Cross and Blue Shield. In stressing the need for a policy of balanced benefits, this committee said, "A benefit structure weighted heavily in favor of either hospital or professional services invariably fosters dissatisfaction. This is reflected not only by initial buyer rejections of contract proposals, but by terminations of contracts due to dissatisfaction with the 'short' coverage in one area or the other. . . .

"We have recognized the often expressed opinion that the stubbornly limited benefits of Blue Shield upset the balance, and the converse opinion that Blue Cross "bids" a coverage which absorbs the bulk of the premium dollar. Both opinions may be valid in given references. . . . The buyer is concerned with the imbalance of benefits in the package, not with the circumstances which caused it . . . particularly when balanced coverages are available from sources other than Blue Cross and Blue Shield."

A discussion of relative value studies and their effects on Blue Shield plan operations produced one of the most interesting sessions of the conference. Drs. H. R. Pezzuti, W. H. Horton, C. D. Moll, and Nicholas F. Alfano, Medical Directors, respectively, of the Pennsylvania, Connecticut, Michigan, and New Jersey Blue Shield plans were the panel members.

Problems discussed included determination of appropriate relative values for nonsurgical procedures and the role of such studies in preventing the public's misunderstandings of fees.

Among the principles set forth in the membership standards adopted by the conference were the following:

1. A plan shall have approval of the state or county medical society, and, if the approving medical society withdraws its approval, such withdrawal shall place a plan's membership on a conditional basis, subject to termination, pending inquiry into the circumstances.

2. Subject to express provisions of law, there shall be free choice by the patient of any duly licensed physician practicing in the area served by the plan.

3. If a plan uses participating physician agreements which affect the benefits provided the subscribers, such plan shall maintain participation of not less than 51% of eligible doctors of medicine practicing in the area served by the plan.

4. The personal relationship between patient and physician shall not be abridged.

5. Benefits may be provided on an indemnity or service basis. Where indemnities are paid to the subscriber, it shall be clearly stated that they are for the purpose of assisting in paying the charges incurred for medical service and do not necessarily cover the entire cost.

6. A plan shall maintain an active program of professional relations directed toward maintaining close cooperation with practicing physicians. This program shall include annual reports of operations and progress to the governing body of the approving medical society, publication of a physicians' manual with all basic information pertinent to the plan's operation, maintenance of a committee or committees of doctors of medicine responsible for review of benefit schedules, review of medical claims requiring individual consideration, and establishment of claims administration policy.

MEDICAL NEWS

DISTRICT OF COLUMBIA

Abel Award to Dr. Mandel.—The American Society for Pharmacology and Experimental Therapeutics has presented the 12th annual Abel award to Harold G. Mandel, Ph.D., associate professor of pharmacology, George Washington University School of Medicine, Washington, D. C. The award, a $1,000 cash honorarium and a bronze medal donated by Eli Lilly and Company, Indianapolis, and sponsored by the society, is named in honor of the late John Jacob Abel, American pharmacologist and founder of the society. To be eligible for the award the candidate "must be under 36 years of age and must have exhibited unusual originality and independence of thought in the conduct of basic research in the field of pharmacology."

GEORGIA

A Medical Family.—Dr. Harold P. McDonald was named president-elect of the Fulton County (Atlanta) Medical Society recently, a few weeks after his brother, Pierce, was elected to the same office in the dental society. Harold is the son of Dr. Paul McDonald, 80-year-old general practitioner, and the father of two physicians, Lawrence and Harold Jr. Lawrence is now serving his internship at U. S. Naval Hospital, Bethesda, Md., and Harold Jr. is interning at Charity Hospital in New Orleans.

IDAHO

State Medical Meeting in Sun Valley.—The 66th annual session of the Idaho State Medical Association will be held July 6-9 at Sun Valley under the presidency of Dr. Hoyt B. Woolley, Idaho Falls. Each of the following guest speakers will present four papers in his specialty: Dr. Don H. O'Donoghue, professor of orthopedic surgery, University of Oklahoma School of Medicine, Oklahoma City; Dr. Horton C. Hinshaw, clinical professor of medicine, Stanford University School of Medicine, San Francisco; Dr. Carl A. Moyer, Bixby professor of surgery, Washington University School of Medicine, St. Louis; Dr. C. Donald Creevy, director, division of urology, University of Minnesota School of Medicine, Minneapolis; and Dr. Ralph C. Benson, professor of obstetrics-gynecology, University of Oregon School of Medicine, Portland. A golf tournament is planned, and facilities are available for tennis, fishing, and other sports. Entertainment includes the president's banquet July 9. For information write Mr. Armand L. Bird, Idaho State Medical Association, 364 Sonna Building, Boise, Idaho.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

State Medical Election.—Dr. Joseph T. O'Neill, pediatrician of Ottawa, has been chosen president-elect of the Illinois State Medical Society, to assume the presidency in May, 1959, when he will succeed Dr. Raleigh C. Oldfield, of Oak Park, who has been installed as president. Other officers elected are: Dr. Lorne W. Mason, Evanston, first vice-president; Dr. Paul P. Youngberg, Moline, second vice-president; and Dr. Harold M. Camp, Monmouth, secretary-treasurer.

Chicago

Dr. Huggins to Receive Cancer Award.—Dr. Charles B. Huggins, professor of urology at the University of Chicago and director of its Ben May Laboratory for Cancer Research, has been named to receive the University of London's third Comfort Crookshank cancer research award, which will be conferred July 3 by Lord Astor of Hever, council chairman of the Middlesex Hospital of the College of Medicine at London in recognition of Dr. Huggins' "fundamental contributions to surgery of cancer." A lecture by Dr. Huggins will follow the presentation. The triennial Crookshank award consists of a silver medal and £250. It has been awarded only twice before, in 1951 to Prof. J. J. Bittner, of the University of Michigan, Ann Arbor, and in 1954 to W. Sampson Handley, of London. Dr. Huggins has been director of the Ben May Laboratory since 1951. On July 7, he will receive from the president of the German Federal Republic its Order "Pour le Merite."

Society News.—At the annual meeting of the Chicago Urological Society the following officers were elected: president, Dr. George O. Baumrucker, Hinsdale; vice-president, Dr. Cornelius W. Vermeulen; and secretary-treasurer, Dr. David Presman.——The Chicago Neurological Society has elected the following officers for 1958-1959: Dr. John J. Madden, president; Dr. Milton Tinsley, vice-president; and Dr. Meyer Brown, Evanston, secretary-treasurer.——At the annual meeting of the

Metropolitan Dermatological Society of Chicago May 14 the following officers were elected: Dr. Henry H. Morrison, president; Dr. Boleslaw K. Lazarski, vice-president; and Dr. Tibor Benedek, secretary-treasurer.

LOUISIANA

Establish Chair in Epidemiology at Tulane.—A chair in epidemiology has been inaugurated at Tulane University of Louisiana School of Medicine by Mr. and Mrs. Charles E. Inbusch, of Milwaukee. The new chair will be known as the Dr. William Hamilton Watkins professorship in epidemiology and is named for the father of Mrs. Inbusch, the former Miss Dorothy Watkins of New Orleans. Dr. Watkins served as chairman of the Yellow Fever Board of New Orleans during the epidemic of 1897. He served as chief inspector of the New Orleans Board of Health and editor of the *New Orleans Medical and Surgical Journal*. He was one of the founders of the Louisiana State Medical Society in 1878 and served as president of the New Orleans Medical and Surgical Association in 1879.

Personal.—Dr. Henry C. Pitot, instructor in Pathology, Tulane University of Louisiana School of Medicine, New Orleans, has been awarded a Lillian Israel Memorial Postdoctoral Fellowship of the American Cancer Society. The fellowship will support the research and training of Dr. Pitot for three years. The grant will enable him to take a doctorate in chemical pathology and to continue research in protein synthesis in normal and cancer tissue under the direction of Dr. Emmanuel Farber, associate professor of pathology and biochemistry.

Society News.—At the annual business meeting of the Louisiana State Society of Anesthesiologists, the following officers were elected: president, Dr. Richard H. Morris, Alexandria; vice-president, Dr. John B. Parmley, New Orleans; and secretary-treasurer, Dr. William E. Trotti, New Orleans.

MAINE

Annual State Meeting in Rockland.—The 105th annual session of the Maine Medical Association will be held June 22-24 at the Samoset, Rockland. A discussion, "Health Insurance Is Here to Stay," June 23 will be followed by a question-and-answer period. The American College of Surgeons, Maine Chapter, will present "Environmental Sepsis" and "Streptococcus Infection in Practice." A panel discussion sponsored by the Maine Medico-Legal Society on the present status of the insanity plea in Maine in homicide cases will be moderated by Judge Charles A. Pomeroy, of Portland. Specialty groups will meet the morning and afternoon of June 24. Entertainment includes the golf tournament and the annual banquet, June 23, 6:30 p.m. For information write the Maine Medical Association, Dr. Daniel F. Hanley, Secretary, P.O. Box 240, Brunswick, Maine.

MASSACHUSETTS

Harvard Students Win Research Awards.—Allan Kliman, of Boston, a fourth-year student at the Harvard Medical School, has received the Soma Weiss award for 1958 for basic research carried on as an undergraduate at the school. His research concerned the mechanism of kidney damage following injection of bacterial extracts. Mr. Kliman's paper was one of seven selected for competition at the 18th annual Undergraduate Assembly of the Harvard Medical School, presented under the auspices of the Harvard Medical Society. Second award in the competition went to Robert Victor Moseley, a third-year student, for basic research in tissue transplantation; Elliot Vesell, a third-year student, received an honorable mention for research on enzyme activity in experimental shock.

Personal.—Dr. Sidney Farber, director of research at Children's Cancer Research Foundation, Boston, and professor of pathology, Harvard University Medical School at The Children's Hospital, has been appointed to serve on the National Advisory Health Council, the Surgeon General of the Public Health Service has announced.——Francis B. Carroll, area medical director of Veterans Administration hospitals and clinics for New England and New York, was given the annual Distinguished Service award by the Massachusetts Elks recently.——The annual Holmes Lecture of the New England Roentgen Ray Society was delivered by Dr. Patrick F. Butler, Boston, on "The Radiologist in Court," May 10.

MISSOURI

Personal.—Dr. Eric Reiss, assistant professor of medicine and preventive medicine and American Cancer Society scholar in medicine at Washington University School of Medicine, St. Louis, has been appointed director of the Irene Walter Johnson Institute of Rehabilitation currently under construction at the medical center. In his new position, Dr. Reiss will plan the program and arrange for the staffing of the institute. Activities of the institute, to be completed in the spring of 1959, will be coordinated through the department of preventive medicine and public health.——Dr. Charles J. Galbraith has been appointed senior instructor in surgery, Saint Louis University School of Medicine and chief of the Saint Louis University Surgical Service at Veterans Administration Hospital in St. Louis.

NEW YORK

State Medical Election.—Dr. Henry I. Fineberg, of Jamaica, was chosen president-elect of the Medical Society of the State of New York by the House of Delegates at the 152nd annual convention and will succeed Dr. Leo E. Gibson, of Syracuse, who was installed as president. Also elected were Dr. Harry Golembe, of Liberty, vice-president; Dr. Joseph A. Lane, of Rochester, speaker; and Dr. Frederick A. Wurzbach, Jr., of the Bronx, vice-speaker. The following were re-elected: Dr. Walter P. Anderton, of New York City, secretary; Dr. Ezra A. Wolff, of Forest Hills, assistant secretary; Dr. Maurice J. Dattelbaum, of Brooklyn, treasurer; and Dr. Samuel Z. Freedman, of New York City, assistant treasurer.

OREGON

University News.—Grants from the U. S. Public Health Service of $157,021 for research projects brought the total of grants received by the University of Oregon Medical School since the first of January to $475,385. Other gifts included $24,100 from the National Science Foundation for research in the division of neurology, $43,728 from the Atomic Energy Commission for research in experimental medicine and biochemistry, $15,000 from the Knights Templar Eye Foundation, $50,555.12 from the Medical Research Foundation of Oregon for studies in various Medical School departments; and $17,600 from the Life Insurance Medical Research Fund to further research on neurohumoral control of kidney functioning.

TEXAS

Workshop on Clinical Chemistry.—A Clinical Chemistry Workshop, sponsored by the Texas Section of the American Association of Clinical Chemists and Baylor University College of Medicine, Houston, will be held in the air-conditioned laboratory of the university's biochemistry department Aug. 18-22. The workshop will be designed to give the participants actual experience in carrying out some of the newer chemical methods useful in the clinical laboratory. The workshop will be open to qualified medical technologists, pathologists, and clinical chemists. Applications will be processed in the order received. Registration fee is $25 (make checks payable to Texas Section, AACC). For information write to the Division of Clinical Chemistry, Department of Biochemistry, Baylor University College of Medicine, Houston 25, Texas.

University News.—Mr. Leslie N. Pyrah, professor of urological surgery, University of Leeds, Leeds, England, presented "Urinary Diversion for Surgical Conditions" at the University of Texas Medical Branch, Galveston, Jan. 22.

WASHINGTON

University News.—Sir Howard W. Florey, 1945 Nobel prize winner, who was cited jointly with the late Sir Alexander Fleming for the discovery of penicillin and is now professor of pathology at the Sir William Dunn School of Pathology at Oxford, spoke at the University of Washington School of Medicine, Seattle, March 17 on the nature of the blood vessel lesion responsible for coronary artery disease.——A bachelor of science degree in physical therapy will now be awarded by the University of Washington, Seattle. The new curriculum will be offered under the department of physical medicine and rehabilitation in the School of Medicine, beginning next fall.

WISCONSIN

A Hobby Becomes a Company.—A hobby, fashioning images of human organs in plastic for tie clasps, cuff links, earrings and key chains, was started by Dr. Robert G. Zach, of Monroe, during World War II and has now developed into a substantial enterprise. He has organized a company which employs nine persons. Dr. Zach is a radiologist at the Monroe Clinic.

Annual Clinical Day.—The 11th annual clinical day of the Marquette University Medical School Dean's Committee will be June 21 at the Veterans Administration Hospital, Wood. The program will open with addresses by Drs. Charles P. Henke, director, professional services at the VA Hospital, and Edward A. Bachhuber, associate dean, Marquette University School of Medicine, Milwaukee. Moderators will be Drs. Joseph P. Looze and Raymond R. Watson. Thirteen papers are scheduled with the following authors: Drs. John J. Frederick (surgery), Reuben Beezy (medicine), Harry D. McGee, (otorhinolaryngology), George J. Owens (radiology), Richard O. Sternlieb (medicine), Jack D. Spankus (orthopedics), Albert M. Cohen (physical medicine), and William R. Taylor (medicine). For information write Dr. Jack J. Levin, Assistant Chief, Medical Service, Veterans Administration Center, Wood, Wis.

Institute of Art Therapy for Mental Patients.—Paintings and drawings created by mental patients in Wisconsin institutions were exhibited at the University of Wisconsin's first Institute of Art Therapy May 18-31, presented by the Wisconsin Psychiatric Institute. The 70 pieces were shown as tools for those who treat patients. Eight of Wisconsin's 37 state and county mental hospitals were represented, and there were pieces from the Northern and Southern Training Colonies for the Mentally Retarded, from the federal Veterans Admin-

istration Psychiatric Hospital at Tomah, and from the Jewish Vocational Service of Milwaukee, a private children's service. The patients ranged in age from 8 to 56. The institute is part of the new teaching program of the Psychiatric Institute, which was founded in 1915 under direction of the late Dr. William F. Lorenz, and became a university agency in 1925.

ALASKA

Dr. Gillett Named Deputy Health Commissioner.—Dr. James A. Gillett, who had been serving in the dual post of Fairbanks city health officer and northern regional health officer for the Alaska Department of Health since August, 1957, became Alaska's deputy commissioner of health, April 1. He came to Alaska last year from Australia, where he had been in private practice since 1951. A native of England, Dr. Gillett received his medical degree from the University of London Guy Hospital Medical School, a diploma in tropical medicine from the University of Edinburgh, and a master of public health from Johns Hopkins University in Baltimore.

GENERAL

Meeting on Vascular Surgery in San Francisco.—The 12th annual meeting of the Society for Vascular Surgery will be held June 22 at the Hotel Sir Francis Drake, San Francisco, with Dr. Frank L. A. Gerbode, president of the society, presiding. Seventeen papers are scheduled for presentation, including "The Rate of Healing of Arterial Autografs in Dogs" by Drs. Hyman Gaylis, and William P. Corvese, and Robert R. Linton. The presidential address, "Some Experiences With Intracardiac Surgery," will be presented by Dr. Gerbode at the luncheon. For information write the Society for Vascular Surgery, 4200 E. 9th Ave., Denver 20, Colo.

Establish Dr. Oughterson Memorial Fund.—The friends of the late Dr. Ashley W. Oughterson have established a memorial fund in the form of a trust "dedicated as a continuing memorial to Dr. Oughterson's work in the field of Medical Education, and to his assistance in the foundation of 'La Clinica de San Miguel Regla' in Mexico." The income from the fund will be used to furnish medical equipment and supplies serving about 4,000 medically indigent people of the Huasca Valley, Mexico. The clinic building, built and presented to the Mayor of Huasca in 1956 by the Club Panamericano de Doctores, has a staff of Mexican senior medical students assigned by their government to tours of duty of about six months. The establishment of the clinic was one of Dr. Oughterson's projects. Contributions may be sent to the Oughterson Memorial Fund in care of Dr. Arthur J. Geiger, 309 Edwards St., New Haven, Conn.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 24, 1958 Paralytic Type	May 24, 1958 Total Cases	May 25, 1957 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	1
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	..	..	1
New Jersey	..	1	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	1	..
Indiana	..	..	..
Illinois	..	..	2
Michigan	..	..	1
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	1	1	..
Missouri	..	..	3
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	4	4
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	..	..	1
West Virginia	..	..	..
North Carolina	1	3	3
South Carolina	..	..	2
Georgia	..	..	1
Florida	1	2	1
East South Central States			
Kentucky	1	2	..
Tennessee	2	3	..
Alabama	..	..	2
Mississippi	..	..	..
West South Central States			
Arkansas	..	1	..
Louisiana	..	..	1
Oklahoma	..	..	..
Texas	5	9	18
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	2
New Mexico	..	..	1
Arizona	..	..	..
Utah	..	1	4
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	3	4	12
Territories and Possessions			
Alaska	..	..	..
Hawaii	1	1	..
Puerto Rico	2	2	..
Total	17	36	61

Annual Conference on Aging.—The University of Michigan, Ann Arbor, will present the 11th annual Conference on Aging June 23-25 at the Michigan Union in Ann Arbor. Four workshops are scheduled: (1) Social Gerontology as a Concept in Aging; (2) Individual Adjustments to Aging; (3) Impact of an Aging Society on the Individual; and (4) Applications of Social Gerontology to Social Action. A panel discussion, "Mobilizing Resources and Maximizing Opportunities," will be held the morning of June 25. Registration fee is $7.50. For information write the Department Extension Service, University of Michigan, 1610 Washtenaw, Ann Arbor, Mich.

Meeting of Catholic Hospital Association.—The 43rd annual convention of the Catholic Hospital Association will be held June 22-26 in Atlantic City, Four general meetings will emphasize the following topics: nursing as an important part of the apostolate, medico-social and economic changes, new concepts of management, and practical consideration of the health of the religious. Special meetings are planned on psychiatry, medical social service, emergency room, control of infection, disaster program, safeguarding newborn life, planning a poison control center, and geriatrics. For information write the Catholic Hospital Association, 1438 S. Grand, St. Louis 4.

Meeting in San Francisco on Angiology.—The fourth annual scientific meeting of the American College of Angiology will be held June 21-22 at the Fairmont Hotel, San Francisco. Two symposiums are planned: "Recent Advances in Cardiovascular Surgery" and "Experimental Angiology," moderated by Dr. Dwight E. Harken and George P. Fulton, Ph.D., respectively. Dr. Sidney S. Rose, consultant and surgeon, University of Manchester, England, will present "Treatment of Leg Ulcers" the afternoon of June 22. Round table discussions will be moderated by Drs. Harken, Rudolph Bircher, and John E. Estes. For information write Alfred Halpern, Ph.D., Secretary, American College of Angiology, 11 Hampton Court, Great Neck, N. Y.

Western Health Departments Win National Award.—The national Samuel J. Crumbine awards, a competition open to over 1,200 local health departments and sponsored by the Public Health Committee of the Paper Cup and Container Institute, New York City, were presented to the City of Spokane Health Department and the Los Angeles City Health Department on May 22 and 23. First place for "outstanding achievement in the development of a program of eating and drinking sanitation" was awarded to Spokane. Top honors for "outstanding achievement in the development of a comprehensive program of environmental sanitation" went to Los Angeles "with special consideration given to newly-developed activities of a pioneering nature which supplement its municipal program." Dr. Hampton H. Trayner, health officer, and Charles K. Reagan, chief general sanitarian of the Spokane Health Department, received personal medallions. Eight awards have been given since the start of the competition, established four years ago to honor Dr. Crumbine, pioneer American public health officer.

Lifetime Investigatorships.—The American Heart Association has announced the appointment of three "career investigators," bringing to six the number of scientists whose research is being supported on a lifetime basis by the association and its affiliates. The new career investigators are David B. Sprinson, Ph.D., professor of biochemistry, Columbia University College of Physicians and Surgeons, New York City; Dr. John V. Taggart, professor of medicine, also at Columbia; and Dr. Lewis W. Wannamaker, associate professor of pediatrics, University of Minnesota Medical School, Minneapolis. Already working as career investigators are Dr. Victor Lorber, University of Minnesota, appointed in 1951, and John R. Pappenheimer, Ph.D., and Dr. Albert H. Coons, both of Harvard Medical School, Boston, and both named in 1953. The career investigatorship is awarded to foster unrestricted research on a lifetime basis by outstanding scientists. Provided with $30,000 a year to cover the investigator's salary and underwrite the expenses of his laboratory, the recipient may work at any institution he selects and he is not obliged to report or publish except when he feels justified in doing so. Dr. Sprinson is working in the general field of intermediary metabolism. Dr. Taggart is a physiologist and biochemist whose chief sphere of interest is the kidney. Dr. Wannamaker's research is concerned primarily with the way in which streptococcal infections apparently "trigger" rheumatic fever. The awards are effective July 1. They bring to 186 the number of individual awards announced by the association and its affiliates for the forthcoming fiscal year, or a commitment of $1,523,000.

Medical Veterans Meeting in San Francisco.—The annual meeting of the National Medical Veterans Society will be held June 21-22 at the Hotel Sheraton–Palace, San Francisco. Dr. Milo A. Youel, president of the society, will address the group the afternoon of June 21. An informal forum June 22, 9.30 a.m., will include the following participants: Major Gen. Paul I. Robinson, (MC) U.S.

Army, director, Medicare; Mr. Thomas A. Hendricks, Field Director, A. M. A.; Dr. Russell B. Roth, Veterans Affairs Committee, A. M. A.; Major Gen. Silas B. Hays, Surgeon General, U.S. Army; Dr. Cyrus H. Maxwell Jr., acting manager, Washington Office, A. M. A.; Dr. Leroy E. Burney, Surgeon General, U.S. Public Health Service; and Rear Adm. B. W. Hogan, Surgeon General, U.S. Navy. For information write Dr. Henry C. Beekley, Secretary, 3117 Warsaw Ave., Cincinnati.

Applications for Heart Research.—Applications by research investigators for support of studies to be developed during the fiscal year beginning July 1, 1959, are being accepted by the American Heart Association. The deadline for Research Fellowship applications and Established Investigatorships is Sept. 15. Applications for grants-in-aid must be made by Nov. 1. Funds for association-supported research in the cardiovascular field are provided by public contributions to the Heart Fund. At least half of all funds received by the American Heart Association's National Office are allocated to research. Almost $31,500,000 has been allocated for research support by the association and its state and local affiliates and chapters in the past 10 years. Applications may be made for awards in the following categories:

Established Investigatorships: Awarded for periods of up to five years, subject to annual review, in amounts ranging from $6,500 to $8,500 yearly plus dependency allowance, "to scientists of proven ability who have developed in their research careers to the point where they are independent investigators." In addition, a grant of $500 is made to the investigator's department.

Advanced Research Fellowships: Awarded for periods of one or two years to postdoctoral applicants "who have had some research training and experience but who are not clearly qualified to conduct their own independent research." During the second year they will be permitted to spend up to 25% of their time in activities not strictly of a research nature, provided that these will contribute to their professional development and do not involve services for a fee. These stipends range from $4,600 to $6,500 annually. A grant of $500 is made to the investigator's department.

Research Fellowships: A limited number of awards is available to young men and women with doctoral degrees for periods of one or two years to enable them to train as investigators under experienced supervision. Annual stipends range from $3,800 to $5,700. This type of award is primarily made by local heart associations.

Grants-in-Aid: Made to experienced investigators to help underwrite the costs of specified projects.

Information may be obtained from the Assistant Medical Director for Research, American Heart Association, 44 East 23rd St., New York 10.

Report of Research Foundation.—In its annual statement for 1957, Research Corporation reported giving $1,257,000 in 364 grants last year, the largest dollar amount in its 46-year history. Since its foundation Research Corporation has granted a total of $12,757,000 for scientific basic research. Research Corporation is a nonprofit foundation established in 1912 by the late inventor-scientist Frederick Gardner Cottrell "to support research in the natural sciences in colleges, universities, and scientific institutions." The foundation receives its funds from its wholly-owned subsidiary, Research–Cottrell, Inc., manufacturer of industrial gas-cleaning equipment in Bound Brook, N. J., and from patents it administers for universities and individual inventors.

A Most-Wanted Fugitive.—Daniel William O'Connor, with aliases Clarence Baker, Daniel Baker, Bob Collins, James Garnie, Marcel Gelinas, Jacob Geres, H. A. Marceaux, Bill O'Brian, Jack O'Brien, Clarence William O'Connor, Bud Rogers, and others. Daniel William O'Connor is one of the FBI's Ten Most Wanted Fugitives. He is being sought for

Most-wanted fugitive.

passing bad checks, and he is a deserter from the United States Army. He is also badly wanted by Canadian authorities on a charge of attempted murder in connection with an assault upon a Royal Canadian Mounted Police Officer. He has been known to travel with his wife, Mary Ursula, age 27, born Sept. 6, 1930, and their two sons, Danny William James O'Connor, age 7, born June 18, 1950, and Jack Kirkland O'Connor, age 6, born Nov. 17, 1951. O'Connor formerly was reported to have degenerative arthritis to a minor degree. His wife has an inguinal hernia on left groin and also has Rh-negative blood factor. Their son, Danny, reportedly has an ugly purplish red scar extending from hairline at center of forehead almost to his right eyebrow. It is requested that if any information comes to your attention concerning these individuals that the nearest office of the Federal

Bureau of Investigation be notified, telephone number of which can be found on the first page of the telephone directory. O'Connor is described as follows: Born Sept. 14, 1928, at Detroit; 5 ft. 7 in. to 5 ft. 9 in.; 200 to 260 lb.; blond hair; blue eyes; ruddy complexion; muscular build; noticeable dimple in chin. This man is known to be armed and considered to be extremely dangerous.

Society News.—The following officers of the **American Society for Surgery of the Hand** will serve for the current year: president, Dr. George V. Webster, Pasadena, Calif.; president-elect, Dr. Julian M. Bruner, Des Moines, Iowa; vice-president, Dr. Daniel C. Riordan, New Orleans; secretary-treasurer, Dr. George S. Phalen, Cleveland; and historian, Dr. Robert M. McCormack, Rochester, N. Y.——The **American Association of Genito-Urinary Surgeons** has elected the following officers: president, Dr. John A. Taylor, New York City; vice-president, Dr. Reed M. Nesbit, Ann Arbor, Mich.; secretary-treasurer, Dr. William J. Engel, Cleveland (reelected); and member of council, Dr. Carl F. Rusche, Los Angeles.——The following officers of the **Industrial Medical Association** have been installed: Dr. Hans W. Lawrence, Cincinnati, president; Dr. Dolor J. Lauer, Pittsburgh, president-elect; Dr. Robert E. Eckardt, Linden, N. J., first vice-president; Dr. John L. Norris, Rochester, N. Y., treasurer; and Dr. Leonard S. Arling, Minneapolis, secretary.——The **North Pacific Society of Neurology and Psychiatry** has elected the following officers: president, Dr. John W. Evans, Portland, Ore.; president-elect, Dr. Jesse L. Henderson, Seattle; secretary-treasurer, Dr. Robert M. Rankin, Seattle; and executive committee: Drs. Robert S. Dow, Portland, Peter O. Lehmann, Vancouver, British Columbia, Canada, and Wallace W. Lindahl, Seattle.——The **American Board of Surgery, Inc.**, has announced that after May 28 its office will be located at 1617 Pennsylvania Blvd., Philadelphia 3.

FOREIGN

Institute for Psychotherapy in Vienna.—An Institute for Psychotherapy has been initiated at the Psychiatric-Neurological Clinic of the University of Vienna, Dr. Hans Hoff, head, department of psychiatry and neurology, and chairman of the institute, announces: Purpose of the institute is "to give a comprehensive survey of modern psychotherapy and to impart theoretical and practical knowledge about all current approaches and techniques of psychotherapy." Various existing training possibilities will be supplemented as the institute will be conducted in close cooperation with university and clinic training facilities. The graduate of the institute is expected to have thorough theoretical and practical knowledge of all psychological treatment methods. The program will be for two years, i. e., four semesters. In the second year the methods of therapy of special groups of patients will be taught. Independent scientific research of the students will be encouraged. Qualified students from other fields can be admitted but are not permitted to take the examinations. For information write Dr. Hans Hoff, Director, Institute for Psychotherapy, Psychiatrisch–Neurologische, Universitatsklinik, Wien IX, Lazarettgasse 14, Austria.

Symposium on Carcinogenesis in London.—The Ciba Foundation will present a symposium, "Carcinogenesis: Mechanisms of Action," June 24-26. Eighteen papers are scheduled, including the following by U. S. participants:

Mechanisms of Carcinogenesis by Viruses, Dr. Jacob Furth, Boston.
Loss of Specific Cell Antigen in Relation to Carcinogenesis, E. C. W. Weiler, Pasadena, Calif.
Relation of Protein-Binding to Hydrocarbon Carcinogenesis, Charles Heidelberger, Ph.D., Madison, Wis.
The Nature of the Neoplastic Transformation in Lymphoid Tumor Induction, Dr. Henry S. Kaplan, San Francisco.
Studies on the Mechanism of Leukemogenesis by Ionizing Radiation, Dr. Arthur C. Upton, Oak Ridge, Tenn.

A reception at the Ciba Foundation will be held June 24 and a dinner, the evening of June 25, at which Professor Sir Macfarlane Burnet, F.R.S., will preside. The annual lecture for 1958 of the Society of Endocrinology will be given by Prof. O. Mühlbock at the Royal Society of Tropical Medicine and Hygiene, London, June 27 on "Hormonal Genesis of Mammary Cancer." For information write the Ciba Foundation, 41, Portland Place, London, W.I.

Turkish Center for Medical Training.—The Rockefeller Foundation has made a two-year grant of $170,000 to the Faculty of Medicine of the University of Ankara, Turkey which is enrolling increasing numbers of students from other Middle Eastern countries. Under a new arrangement, fees for the foreign group—about 25 out of each entering class—will be paid by the Turkish government. Until recently the medical curriculum at Ankara followed a traditional pattern. Two years ago the faculty inaugurated a system in the department of child health based on smaller classes and more laboratory and hospital experience, and then went on to incorporate similar changes in all the basic science and clinical departments. In the basic science courses students now spend two-thirds of their time in the laboratory and one-third in the lecture room. In their clinical years they divide into small groups for clinical and theoretical training and under a "clinical clerkship" requirement take medical histories, conduct physical examinations, as-

sist at obstetrical deliveries, and perform other professional services under supervision. The foundation's grant will enable the faculty to purchase additional equipment and supplies outside Turkey. The Rockefeller Foundation in 1956 made a $100,000 grant to the university in support of its program in pediatrics.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

ARIZONA:* *Examination.* Phoenix, July 16-18. *Reciprocity.* Phoenix, July 19. Sec., Dr. Thomas N. Bate, 826 Security Bldg., Phoenix.

CALIFORNIA: *Written Examination.* Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, June 14; Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

CONNECTICUT:* *Examination.* Hartford, July 8-10. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DELAWARE: *Examination and Reciprocity.* Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

FLORIDA:* *Examination.* Miami, June 29-July 1. Sec., Dr. Homer L. Pearson, 901 N. W. 17th St., Miami.

IDAHO: *Examination.* Boise, July 14-16. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Written Examination.* Chicago, July 7-11. *Oral Reciprocity Examination.* Chicago, July 11. Supt. of Regis., Mr. Frederic Selcke, Capitol Bldg., Springfield.

MAINE: *Examination.* Augusta, July 8-10. *Reciprocity.* Augusta, July 8. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

MASSACHUSETTS: *Examination.* Boston, July 15-18. Sec., Dr. Robert C. Cochrane, Room 37 State House, Boston.

MISSISSIPPI: *Examination.* Jackson, June 23-24. *Reciprocity.* Jackson, June 25. Asst. Sec., Dr. R. N. Whitfield, Old Capitol Bldg., Jackson 113.

MONTANA: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEW HAMPSHIRE: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

NEW YORK: *Examination.* Albany, Buffalo, New York City and Syracuse, June 24-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Reciprocity.* Blowing Rock, July 25. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OREGON:* *Examination.* Portland, July 16-17. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July 8-10. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, June 26-27. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 24-25. Sec., Dr. H. E. Jervey, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 23-25. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination.* Salt Lake City, July 9-11. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

WASHINGTON:* *Examination.* Seattle, July 14-16. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WEST VIRGINIA: *Examination and Reciprocity.* Charleston, July 14-16. Sec., Dr. N. H. Dyer, State Office Bldg., No. 5, Charleston.

WISCONSIN:* *Examination.* Milwaukee, July 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

WYOMING: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

HAWAII: *Examination.* Honolulu, July 14-15. Sec., Dr. I. L. Tilden, 1029 Kapiolani St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

ARKANSAS: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

COLORADO: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

IOWA: *Examination.* Des Moines, July 8. *Reciprocity.* Des Moines, July 7. Sec., Dr. Elmer W. Hertel, Waverly.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

NEW MEXICO: *Examination.* Santa Fe, July 20. *Reciprocity.* Santa Fe, June 26. Sec., Mrs. M. Cantrell, P. O. Box 1522, Santa Fe.

OKLAHOMA: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

TENNESSEE: *Examination.* Memphis, July 1-2. Sec., Dr. O. W. Hyman, 62 S. Dunlap St., Memphis.

TEXAS: *Examination.* October. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination. Madison,* Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

*Basic Science Certificate required.

GOVERNMENT SERVICES

ARMY

Second Army Conference.—At the Second Army Civilian Medical Consultants' and Hospital Commanders' Conference at Fort George G. Meade, Md., May 28-29, called by Col. Francis P. Kintz, Second Army Surgeon, Dr. Manfred S. Guttmacher, chief medical officer, Medical Service of the Supreme Bench of Baltimore, talked on military psychiatry and criminology, and Dr. M. P. Hilleman, director of virus research, Merck, Sharpe & Dohme, talked on respiratory disease. Among the military guests were Major Gen. J. P. Cooney, Army deputy surgeon general, and Major Gen. I. S. Ravdin, retired, chairman, Second Army Civilian Consultants' Advisory Committee. The conferees included Second Army area hospital commanders with their chiefs of medical and surgical services, other representatives of the surgeon general's office, and civilian consultants assigned to headquarters, Second Army, and to Army hospitals in the Second Army area.

NAVY

Hospital Corpsman Selects Unknown Serviceman of World War II.—William R. Charette of Ludington, Mich., hospital corpsman first class, the only enlisted man on active duty in the Navy holding the Congressional Medal of Honor, was designated to select the World War II Unknown Serviceman to be committed to Arlington National Cemetery on Memorial Day, 1958. Charette, aboard the cruiser Canberra on May 26, in a ceremony off Norfolk, Va., made the selection from the remains of two unknown servicemen, previously selected in Epinal, France, and Honolulu who symbolize the Americans who died unidentified in European Operations and Pacific Operations during World War II.

The body of the Unknown Serviceman of the Korean war (selected in Honolulu on May 15), along with the World War II choice, was then transferred to Arlington National Cemetery for burial May 30, next to the Unknown Soldier of World War I. Both men lay in state in the Capitol Rotunda in Washington, D. C., before the Arlington ceremonies.

Charette, who is presently serving aboard the U. S. S. Quillback, was with the First Marine Division at the time he was cited during the Korean war for conspicuous gallantry. He was decorated by President Eisenhower at a White House ceremony on Jan. 12, 1954.

VETERANS ADMINISTRATION

Hospital Managers Transferred.—Transfer of five hospital managers has been announced.

Dr. Claud E. Carter, manager, VA Hospital, Butler, Pa., will become manager of the Fresno, Calif., VA Hospital, replacing Dr. Forrest G. Bell, who is retiring. Dr. Roland W. Hipsley, manager of the New Orleans VA Hospital, will be reassigned as manager of the Butler Hospital. Dr. Thomas L. Harvey, manager, VA Hospital, Montgomery, Ala., will become manager of the New Orleans Hospital.

Dr. Daniel H. Miller, manager, VA Hospital, Muskogee, Okla., will replace Dr. Harvey at Montgomery. To fill the vacancy at Muskogee, Dr. Alexander W. Kruger, manager, VA Hospital, Brooklyn, N. Y., will be transferred as manager. Dr. Henry L. Schmidt Jr., director, professional services, VA Manhattan Hospital in New York City, has been appointed manager of the Brooklyn Hospital.

PUBLIC HEALTH SERVICE

Dr. Lowry Appointed Assistant Surgeon General.—Dr. James V. Lowry has been appointed as chief of the Bureau of Medical Services with the rank of assistant surgeon general, succeeding Dr. John W. Cronin who died on March 26. The Bureau of Medical Services administers the Public Health Service hospitals, the Indian Health Service, Foreign Quarantine, the Hospital Survey and Construction Program, and research activities concerned with the nation's dental and nursing resources. Dr. Lowry, who entered the Public Health Service in 1937, is a diplomate of the American Board of Psychiatry and Neurology, and a past-president of the Kentucky Psychiatric Association.

Personal.—Dr. Arnold B. Kurlander has been appointed deputy chief of the Public Health Service Bureau of Medical Services. The bureau is responsible for administering Public Health Service hospitals, the Indian Health Service, Foreign Quarantine, the Hospital Survey and Construction Program, and research activities concerned with the nation's dental and nursing resources. He will succeed Dr. James V. Lowry, who has been named chief of the bureau. Dr. Kurlander has been a member of the Commissioned Corps since 1940.

DEATHS

Andrew, Richard M., New York City; New York Homeopathic Medical College and Hospital, New York City, 1891; died April 15, aged 97.

Armstrong, Arthur, Springfield, Mo.; Missouri Medical College, St. Louis, 1896; died April 5, aged 92, of senility.

Benz, Henry John, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1904; an associate member of the American Medical Association; for many years chief of the city's school health service and superintendent of the bureau of child welfare; senior staff pediatrician, St. Joseph's Hospital, where he died April 4, aged 75, of bronchopneumonia, cerebral thrombosis, and gangrenous cholecystitis.

Blunck, Conrad Frederick Ernst, New York City; Columbia University College of Physicians and Surgeons, New York City, 1923; associated with St. Elizabeth's Hospital; died in Nyack (N. Y.) Hospital Feb. 2, aged 69, of coronary occlusion.

Box, William Lyles ✦ Vernon, Ala.; Medical College of Alabama, Mobile, 1906; for many years county health officer; died April 1, aged 75, of cerebral hemorrhage.

Boyce, Samuel Robert ✦ Gays Mills, Wis.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; fellow of the American College of Surgeons; died in Madison April 1, aged 95, of bronchopneumonia and cerebral vascular accidents.

Brake, John W., Cumberland Furnace, Tenn.; University of Tennessee Medical Department, Nashville, 1891; died in Clarksville April 1, aged 92, of a fractured hip.

Brittain, Oman R. ✦ Salina, Kan.; John A. Creighton Medical College, Omaha, 1903; specialist certified by the American Board of Radiology; member of the American College of Radiology; veteran of World War I; on the staffs of St. John's and Asbury hospitals; died in St. Francis Hospital, Wichita, April 3, aged 79, of uremia.

Brown, Robert Dwight, East New Market, Md.; National Medical University, Chicago, 1897; an associate member of the American Medical Association; veteran of World War I; at one time associated with the U. S. Public Health Service Reserve and the Veterans Bureau; died March 31, aged 84.

✦ Indicates Member of the American Medical Association.

Cusack, Thomas Stanislaus ✦ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1915; served on the staffs of Central Islip (N. Y.) State Hospital, Kings Park (N. Y.) State Hospital, and Samaritan Hospital; died April 14, aged 74.

Davison, Hal McCluney ✦ Atlanta, Ga.; born in Woodville Oct. 2, 1891; Atlanta Medical College, 1915; for many years on the faculty of his alma mater, now Emory University School of Medicine; specialist certified by the American Board of Internal Medicine; past-president of the Southeastern Allergy Association, Medical Association of Georgia, American Therapeutic Society, and the Fulton County Medical Society; member of the American College of Allergists, of which he was past-president, and the American Academy of Allergy; fellow of the American College of Physicians; during World War I served with the U. S. Army, American Expeditionary Force in Siberia, where he worked with the American Red Cross the following year; trustee of the Mercer University, Macon; formerly on the staff of the Emory University Hospital, Grady Memorial Hospital, St. Joseph's Infirmary, and Crawford W. Long Hospital; for many years chief of medicine at the Georgia Baptist Hospital, where he died April 26, aged 66, of Hodgkin's disease and peritonitis.

Ellis, Leland Wadsworth, San Marino, Calif.; Stanford University School of Medicine, San Francisco, 1921; assistant professor of surgery at College of Medical Evangelists, Loma Linda and Los Angeles; an associate member of the American Medical Association; fellow of the American College of Surgeons; served on the staffs of the Alhambra (Calif.) Community Hospital, Garfield Hospital in Monterey Park, and St. Luke and Collis P. and Howard Huntington Memorial hospitals in Pasadena; died in San Gabriel April 10, aged 61, of coronary thrombosis.

Ensley, Bruce ✦ Shell Rock, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; died in the St. Joseph Mercy Hospital, Waverly, March 6, aged 79.

Estrin, Morris M. ✦ Brooklyn; University of Colorado School of Medicine, Denver, 1923; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; served on the staffs of the Kings County and Adelphi hospitals; died in the Flower and Fifth Avenue Hospitals in New York City April 18, aged 58, of cancer.

Farrell, Martin Joseph, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1918; member of the medical staff at Misericordia Hospital, where he died April 8, aged 67, of cerebral thrombosis.

Fox, Denton Bernard, Grosse Pointe Park, Mich.; Loyola University School of Medicine, Chicago, 1937; died in the Jennings Memorial Hospital, Detroit, Feb. 3, aged 46, of cancer of the esophagus with metastasis to liver.

Furrer, Helen Hempstead, Cleveland Heights, Ohio; Johns Hopkins University School of Medicine, Baltimore, 1905; died Feb. 2, aged 78.

Gill, George, Elyria, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1896; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; associated with the Elyria Memorial Hospital, where he died April, aged 92, of cerebral thrombosis due to arteriosclerosis.

Green, Otto Ishmael ✱ Bartlesville, Okla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; on the staff of the Jane G. Phillips Memorial Hospital; died in Sand Springs April 4, aged 79, of lung cancer.

Hargreaves, Oliver Cromwell ✱ Denver; Northwestern University Medical School, Chicago, 1904; veteran of World War I; died March 27, aged 85, of lobar pneumonia and cancer.

Harrigan, Thomas Joseph ✱ Altoona, Pa.; Temple University School of Medicine, Philadelphia, 1937; member of the staff of the Mercy Hospital; died April 1, aged 46.

Harris, Clarence Newton, Indianapolis; Meharry Medical College, Nashville, Tenn., 1900; for many years city school physician; died April 6, aged 83, of cerebral thrombosis.

Heath, John Francis, Dayton, Ohio; Eclectic Medical College, Cincinnati, 1918; member of the Ohio State Medical Association; on the courtesy staff, Good Samaritan Hospital, where he died April 3, aged 71, of cerebral vascular accident.

Hendrick, Rhoda Grace, Tucson, Ariz.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; died April 3, aged 83, of bronchopneumonia, congestive heart failure, and arteriosclerotic heart disease.

Johannesson, Carl John ✱ Portland, Ore.; born in Copenhagen, Denmark, March 29, 1891; Loyola University School of Medicine, Chicago, 1917; for many years practiced in Walla Walla, Wash., where he was past-president of the Walla Walla Valley Medical Society; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Washington State Medical Association, and the Radiological Society of North America; veteran of World Wars I and II; for many years was associated with the Veterans Administration Hospital, Washington State Penitentiary, St. Mary's Hospital, and Walla Walla General Hospital, all in Walla Walla; died March 28, aged 66, of cancer.

Johnston, Florence Dorothy ✱ Cedar Rapids, Iowa; University of Pennsylvania School of Medicine, Philadelphia, 1919; member of the American Society of Anesthesiologists; charter member of Iowa Anesthesiological Society; became librarian on July 1, 1923, of the American Medical Association and the following year assistant editor of THE JOURNAL, resigning in 1925 from this staff; associated with Mercy and St. Luke's Methodist Hospitals; died April 5, aged 65, of cerebral thrombosis.

Kaess, Andrew Joseph, Berkeley, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; veteran of World War I; at one time practiced in Moorhead, Minn., where he was coroner of Clay County, and at Fargo, N.D., where he was associated with St. John's Hospital; died April 11, aged 79.

Kampschmidt, August William ✱ Bethlehem, Pa.; University of Missouri School of Medicine, Columbia, 1906; for many years practiced medicine in Columbia, Mo.; where he served as city health officer; member of the Missouri State Medical Association; died in St. Luke's Hospital April 7, aged 82.

Kelly, Harvey Augustine ✱ Winthrop, Mass.; born in 1883; Baltimore Medical College, 1906; member of the American Academy of General Practice; past-president of the Massachusetts Academy of General Practice; past vice-president and for 20 years councilor of the Massachusetts Medical Society; past-president of the Suffolk District Medical Society; served on the hospital advisory board of the State Department of Public Health; veteran of World Wars I and II; served as medical director of the Winthrop public schools; one of the founders of Winthrop Community Hospital and served as its executive chairman for many years and president of its medical staff for five years; on the staff of the Chelsea (Mass.) Memorial Hospital; formerly staff member, Whidden Memorial Hospital in Everett; president of the Winthrop Cooperative Bank; member of the editorial board, *The New England Journal of Medicine;* died in the Phillips House, Massachusetts General Hospital April 8, aged 75, of pulmonary edema.

King, Ernest Harold, Tujunga, Calif.; Jefferson Medical College of Philadelphia, 1914; an associate member of the American Medical Association; veteran of World War I; died in Santa Monica March 24, aged 67.

King, Harry Clifton, Washington, D.C.; Hahnemann Medical College and Hospital of Philadelphia, 1907; veteran of World War I; associated with the Hahnemann Hospital; died April 16, aged 73, of acute congestive heart disease.

Klaer, Clarence, Lock Haven, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1896; an associate member of the American Medical Association; died in the Geisinger Memorial Hospital, Danville, April 11, aged 84, of cardiac failure.

Klostermann, George William ✦ Irvington, Ill.; Homeopathic Medical College of Missouri, St. Louis, 1907; died April 7, aged 82, of coronary occlusion.

Knight, Robert Allen ✦ Memphis, Tenn.; born in Carter, Okla., Nov. 21, 1914; University of Oklahoma School of Medicine, Oklahoma City, 1938; assistant professor of orthopedic surgery at University of Tennessee College of Medicine; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association, American Academy of Orthopaedic Surgeons, and Clinical Orthopaedic Society; fellow of the American College of Surgeons; president of the American Academy of Cerebral Palsy, which he served as secretary-treasurer; associated with the Campbell Clinic Hospital, Hospital for Crippled Adults, Crippled Children's Hospital School, Baptist Memorial Hospital, Le Bonheur Children's Hospital, Methodist Hospital, St. Joseph Hospital, and U. S. Public Health Service Hospital; joint editor of the third edition of "Campbell's Operative Orthopedics"; died in Walnut Grove, Miss., April 13, aged 43, of injuries received in an automobile accident.

Leever, William Edward, Cincinnati; Medical College of Ohio, Cincinnati, 1901; died April 4, aged 83, of arteriosclerosis.

Levy, Albert Lewis, New York City; Cornell University Medical College, New York City, 1911; member of the Medical Society of the State of New York; specialist certified by the American Board of Orthopaedic Surgery; associated with the Hospital for Joint Diseases and Jewish Memorial Hospital, where he served as president of the medical board; died April 12, aged 68, of emphysema.

Lossow, Meyer Joseph, Alamo, Calif.; Cornell University Medical College, New York City, 1919; died March 28, aged 64.

Low, Victor, Honesdale, Pa.; Columbia University College of Physicians and Surgeons, New York City, 1899; served on the staff of the Farview State Hospital in Waymart; died March 18, aged 79, of heart disease.

Lucas, William Henry Sr. ✦ Cedartown, Ga.; University of Louisville (Ky.) Medical Department, 1909; died in Atlanta March 25, aged 80.

Lull, Cabot ✦ Birmingham, Ala.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; specialist certified by the American Board of Internal Medicine; past-president of the Jefferson County Medical Society; veteran of World War I; for many years medical director of the Anti-Tuberculosis Association of Jefferson County; associated with the Jefferson Tuberculosis Sanitorium, where he was past-president of the board and where, in 1953, the education building was named for him, South Highland Infirmary, and St. Vincent's Hospital; died March 31, aged 83.

McCarthy, Harriet Cecilia Schwartz ✦ Kankakee, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; specialist certified by the American Board of Psychiatry and Neurology; associated with the Kankakee State Hospital, where she died March 25, aged 69, of coronary occlusion and hypertension.

Manion, Edward Bartholomew, Ilion, N.Y.; Albany (N.Y.) Medical College, 1910; for many years county coroner; served on the staff of the Ilion Hospital; died March 15, aged 70, of coronary embolism.

Martin, Zeno Thomas ✦ Austin, Texas; University of Texas School of Medicine, Galveston, 1920; veteran of World War I; formerly city health officer; served on the staff of the Austin State Hospital; died March 28, aged 61.

O'Neal, Martha Margaret ✦ Zanesville, Ohio; Western Reserve University School of Medicine, Cleveland, 1930; member of the American Academy of Pediatrics; past-president of the Muskingum County Medical Society; served as county health commissioner; associated with Good Samaritan and Bethesda hospitals; died in Cleveland Clinic Hospital March 28, aged 54, of aneurysm.

Orr, William H., Ventnor, N. J.; University of Louisville (Ky.) Medical Department, 1894; died Feb. 17, aged 88.

Papez, James Wenceslas ✦ Columbus, Ohio; University of Minnesota College of Medicine and Surgery, Minneapolis, 1911; served on the faculty of Cornell University in Ithaca, N.Y.; at one time on the faculty of Emory University School of Medicine in Atlanta, Ga.; member of the Association for Research in Nervous and Mental Disease; director of the laboratory for biological research, Columbus State Hospital; died April 13, aged 74.

Pavlinac, Joseph Henry ✦ Macomb, Ill.; George Washington University School of Medicine, Washington, D.C., 1925; died April 18, aged 57, of coronary thrombosis.

Pedersen, Victor Cox, Kensington, Md.; born in New York City Nov. 15, 1867; Columbia University College of Physicians and Surgeons, New York City,

1898; founder member of the American Board of Urology; in 1910 member of the House of Delegates of the American Medical Association; served as secretary and chairman of the genitourinary section of the New York Academy of Medicine; member of the American Urological Association and served as treasurer, vice-president, and president of the New York Society; member of the Society of Medical Jurisprudence, Society for Advancement of Clinical Research, Association of Military Surgeons of the United States, Military Order of Foreign Wars of the United States, and many other societies; fellow of the American College of Surgeons; an associate member of the American Medical Association; veteran of World War I; for many years practiced in New York City, where he was associated with St. Mark's Hospital; author of numerous books and articles on urology and sociology; died in the Le Deau Gardens Sanitarium in Forest Glen April 9, aged 90, of congestive heart disease.

Perrin, William, Rochester, N.Y.; New York Homeopathic Medical College and Hospital, New York City, 1901; associated with the Genesee Hospital, where he died April 7, aged 82, of nephrosclerosis.

Pope, Samuel Byron ✙ Norfolk, Va.; Medical College of Virginia, Richmond, 1930; member of the American Academy of General Practice; on the staffs of the Norfolk General, Leigh Memorial, and DePaul hospitals; died April 2, aged 53, of a heart attack.

Preuss, Joseph George, New York City; Schlesische–Friedrich–Wilhelms–Universität Medizinische Fakultät, Breslau, Prussia, Germany, 1921; member of the Medical Society of the State of New York and the American College of Gastroenterology; on the staff of the Metropolitan Hospital; died March 30, aged 63, of coronary thrombosis.

Purcell, Ernest Francis Jr. ✙ Trenton, N.J.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1947; certified by the National Board of Medical Examiners; member of the American Society of Anesthesiologists; veteran of the Korean War; associated with McKinley Memorial Hospital, where he died April 5, aged 36, of leukemia.

Read, Wilmot Deleo ✙ Tacoma, Wash.; Cooper Medical College, San Francisco, 1903; fellow of the American College of Surgeons; past-president of the Pierce County Medical Society and the Washington State Medical Association; served overseas during World War I; first president of the Pierce County Medical Service Bureau and past-president of the Washington State Medical Bureau, which he helped found, predecessor of Washington Physicians Service; associated with the Tacoma General Hospital; died April 3, aged 78, of cerebral thrombosis.

Reils, Edwin August, Palmer, Neb.; University of Nebraska College of Medicine, Omaha, 1923; died in the Immanuel Hospital, Omaha, Feb. 16, aged 64, of cerebral hemorrhage.

Rice, Franklyn Augustus, Niles, Mich.; born in North Olmsted, Ohio, June 30, 1885; University of Wooster Medical Department, Cleveland, 1909; fellow of the American College of Surgeons; served overseas during World War I and later with the Army of Occupation; veteran of World War II and in 1946 was awarded the Legion of Merit for "his superior performance of duty as chief of the surgical service, Billings General Hospital, Fort Harrison, Ind., from March 25, 1943, to Dec. 3, 1945"; formerly practiced in Cleveland, where he was associated with the St. Vincent Charity and St. Luke's hospitals; associated with the Pawating Hospital; died April 9, aged 72, of lung cancer.

Root, Raymond Richmond ✙ Georgetown, Mass.; Harvard Medical School, Boston, 1914; veteran of World War I; for many years school physician; on the staff of the Hale Hospital, Haverhill, where he died April 3, aged 76, of coronary occlusion and emphysema.

Ruhland, George Clemens ✙ Washington, D.C.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1904; at one time on the faculty of his alma mater; veteran of World War I; served as commissioner of health of Milwaukee, Syracuse, N. Y., and the District of Columbia; formerly secretary-treasurer of the District of Columbia Commission on Licensure, and secretary of the Association of State and Territorial Health Officers; died in the Providence Hospital April 15, aged 79, of coronary heart disease.

Shnayerson, Edward Felix ✙ Brooklyn; Cornell University Medical College, New York City, 1928; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War II; associated with Coney Island and Maimonides hospitals, and the Caledonian Hospital, where he died April 10, aged 55.

Sloan, William Henry, Garland, N. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; member of the Medical Society of the State of North Carolina; veteran of World War I; on the staff of the Sampson County Memorial Hospital in Clinton; died in Durham April 9, aged 67, of heart disease.

Smith, Charles Enion ✙ Chicago; Loyola University School of Medicine, Chicago, 1918; member of the American Academy of General Practice; on the staff of the Ravenswood Hospital; died April 21, aged 70, of cerebral hemorrhage, arteriosclerosis, and hypertension.

Smith, Harry Theopilus, Elverson, Pa.; George Washington University School of Medicine, Washington, D.C., 1904; past-president of the Chester County Medical Society; veteran of the Spanish-American War and World War I; served on the staff of the Pottstown (Pa.) Hospital; died in Pottstown April 15, aged 85, of uremia.

Snover, Clayton Halsey, Randolph, N.Y.; University of Buffalo School of Medicine, 1908; an associate member of the American Medical Association; served on the staffs of the Jamestown General Hospital and the Woman's Christian Association Hospital in Jamestown, where he died April 11, aged 75, of acute hemorrhagic pancreatitis.

Sullivan, Eugene Shaw, Madison, Wis.; Columbia University College of Physicians and Surgeons, New York City, 1918; fellow of the American College of Surgeons; on the staffs of the Madison General and St. Mary's hospitals; died April 8, aged 63.

Swan, James Hayes, Chambersburg, Pa.; Jefferson Medical College of Philadelphia, 1903; an associate member of the American Medical Association; past-president of the Franklin County Medical Society; associated with Chambersburg Hospital; died March 29, aged 85, of cerebral thrombosis.

Taylor, James Boyce, Huntington, W. Va.; Baltimore Medical College, 1894; in 1894 elected to the state legislature, and again in 1926 served as a state senator; formerly mayor of Huntington; served as president of the county board of health; formerly on the staff of the Chesapeake and Ohio Railway Hospital; died April 2, aged 89.

Thomas, Arthur W., Springfield, Mo.; University Medical College of Kansas City, Mo., 1895; died April 1, aged 86.

Thornburg, Maurice Redfield, Chicago; Northwestern University Medical School, Chicago, 1924; died in the Illinois Central Hospital April 6, aged 63.

Walker, Gale Havard ✙ Polk, Pa.; University of Pittsburgh School of Medicine, 1930; member of the American Psychiatric Association; past-president of the Association of Mental Deficiency; formerly an officer in the regular Army; superintendent of the Polk State School; died April 22, aged 52, of acute coronary occlusion.

Wallerstein, Arthur Albert ✙ Chicago, Ill.; Kaiser–Wilhelms–Universitat Medizinische Fakultät, Strassburg, Germany, 1902; veteran of World War I; on the staff of the Edgewater Hospital, where he died April 27, aged 79, of acute peritonitis with abscess and cancer of the gallbladder.

Weiss, Edward Hervey, Philadelphia; Jefferson Medical College of Philadelphia, 1927; member of the Medical Society of the State of Pennsylvania; associated with the Doctors and Misericordia hospitals; died in the Graduate Hospital of the University of Pennsylvania April 12, aged 54, of arteriosclerotic cardiovascular disease.

Wentz, Irl Zeigler ✙ Seaside Heights, N.J.; Jefferson Medical College of Philadelphia, 1920; member of the American Academy of General Practice; school physician; died in Newport, N.C., April 5, aged 61, of a heart attack.

Wieters, John Christopher, Asheville, N. C.; Medical College of South Carolina, Charleston, 1912; member of the Medical Society of the State of North Carolina; died March 16, aged 67, of chronic myocarditis and arteriosclerosis.

Wilson, Robert Lee ✙ Surgeon, U.S. Public Health Service, retired, Austin, Texas; University of Texas School of Medicine, Galveston, 1898; service member of the American Medical Association; retired from the U.S. Public Health Service in 1933; later employed as ship's doctor for several different steamship companies, principally the United Fruit Company; died April 1, aged 87.

Wittenberg, Harry J., Cincinnati; Cincinnati College of Medicine and Surgery, 1901; member of the Ohio State Medical Association and the American Trudeau Society; died April 4, aged 78.

Wood, Horatio C. Jr., Philadelphia; born in Philadelphia Feb. 26, 1874; University of Pennsylvania Department of Medicine, Philadelphia, 1896; emeritus professor of therapeutics at his alma mater and the University of Pennsylvania Graduate School of Medicine; emeritus professor of pharmacology at the Philadelphia College of Pharmacy and Science; chairman, Section on Pharmacology and Therapeutics, American Medical Association, 1906-1907; for many years member of the Committee of Revision of the United States Pharmacopoeia and served as vice-president of the United States Pharmacopoeial Convention; editor emeritus of "Dispensatory of the United States of America"; died March 31, aged 84, of cardiac failure.

Wright, Solon Westcott ✙ Bessemer, Ala.; Birmingham Medical College, 1911; member of the American Acedemy of General Practice; veteran of World War I; died in Birmingham March 21, aged 73.

Wucher, Frederick Vaux ✙ Pittsburgh; University of Pittsburgh School of Medicine, 1925; died in St. Francis General Hospital April 2, aged 60, of coronary thrombosis.

Zack, Arno Roy, Bethlehem, Pa.; Medico-Chirurgical College of Philadelphia, 1915; an associate member of the American Medical Association; on the staff of St. Luke's Hospital, where he died March 29, aged 67, of acute posterior myocardial infarction.

FOREIGN LETTERS

BRAZIL

Influenza and Antibiotics.—Dr. F. C. Algodoal (*Arquivos Médicos Municipais,* March, 1958) made no claim that antihistaminics prevent influenza, but they decrease susceptibility by eliminating an allergic component. Even if they do not inhibit the allergic component which facilitates infection, they may reduce congestion, edema, and coughing. Some antihistaminics also have a tranquilizing action and induce calm sleep. No known antibiotic is effective against influenza but penicillin V may be given by mouth to prevent secondary bacterial invasion.

Burns.—Dr. A. do Carmo Russo (*Revista Paulista de Medecina,* March, 1958) analyzed a series of 1,678 burned patients and found an increase in the incidence of burns from 0.32 per 1,000 in the period 1948 to 1951 to 0.62 per 1,000 in the period 1955-1956. The incidence of burns in children was 1.20 per 1,000 inhabitants, compared with 0.38 per 1,000 in adults. In this series 56.25% of the patients were under 15 years of age. Most of the patients (92.62%) were burned in or near home. In 64.2% the burns occurred in the kitchen. The incidence was greatest in the colder months and was greatest in housewives (50.38%). In 17.43% of the cases, more than one person was burned in the accident. Many burns were caused by explosion of alcohol burners or pressure cookers. Lesions caused by burning clothing occurred chiefly in girls. A great decrease was noted in accidents caused by firecrackers.

CANADA

Supply of Physicians.—Dr. R. R. Struthers (*Canadian Medical Association Journal,* April 1, 1958) endeavored to show that Canada has an oversupply of medical schools, that several of these schools are hard pressed to recruit sufficient numbers of adequately prepared students, and that the present national population does not warrant 12 medical schools in terms of money for salaries of teachers and equipment or amount of teaching material. The population-physician ratio has remained constant in spite of the fact that almost 25% of the annual graduating class from Canadian medical schools eventually practice in the United States. Taking the average expectation of life for men 27 years of age, it may be assumed that the present number of 16,000 Canadian physicians will require replacement at about 3% per annum to compensate for deaths and retirements. Of the present 16,000, therefore, about 11,000 will still be in practice in 1965. If to this figure are added 800 graduates per annum for 10 years (the present graduation rate minus the loss to the United States) together with about 200 immigrants per annum, there will be a total of 10,000 added to the list, giving a grand total of 21,000 doctors in 1965. This number, on the basis of population forecasts, would be adequate.

Some valid objections may be made to these calculations. For example, the calculation should not be based on an average expectation of life at age 27, for it seems that at present there is a great hump in the physician population at around 45 years of age. This means that in 20 years there will be a mass retirement of physicians beyond the ordinary attrition. Moreover, no one can tell what demands will be made on the profession by the introduction of hospital insurance, possibly supplemented by further insurance benefits to the general population. The deans of medical schools, however, are worried not about the quantity but about the quality of applicants to their schools.

Hospital Insurance.—The federal government has got the requisite six provinces to participate in the Federal-Provincial Universal Hospital Insurance Scheme. Of the remaining four all but Quebec are also falling into line. Manitoba is the latest to announce its plans, and although they have been slow in appearing, the start of this scheme is being hastened, and it should become effective in July. The scheme does not differ greatly from that announced by Ontario. It provides standard (public) ward accommodation with no time limit; necessary nursing services; laboratory, roentgenographic, and other diagnostic services; drugs, biologicals, and related preparations; use of operating room; anesthetic facilities; routine surgical supplies; radiotherapy; and physiotherapy. Like Ontario's scheme, it covers emergency services for injured persons on an outpatient basis within 24 hours of an accident. Manitoba has managed to shave 5 cents a month off the Ontario cost, for the basic cost in premiums will be $2.05 for an individual and $4.10 for a family. The government will carry the cost for the first six months, the premiums starting on Jan. 1, 1959. Social security cases will be covered free. Mental and tuberculous patients are also given full hospital coverage, although the federal government does not include this service in its plan. Costs of this additional service will be borne by the province. There will be no deterrent charges, deductible

The items in these letters are contributed by regular correspondents in the various foreign countries.

clauses, restrictions against age, or time limits. Firms employing five or more persons will register their employees and collect the premiums. Self-employed and other persons will register at municipal offices. Any person laid off work and having his premiums paid up to date will have his hospital insurance continue in force for at least six months after his layoff. The scheme is compulsory, and anyone who fails to join may be fined up to $200.

Medical Bacteriology.—The medical bacteriologists of Canada are worried about their current status. The recruitment of young medical graduates into this specialty has been poor of late. The broad field of bacteriology, including virology, mycology, and parasitology, is inadequately covered by the 78 medically qualified bacteriologists of Canada, even with recruitment from Europe. There is no doubt that further demands will be made on the specialty when the hospital insurance scheme begins. Lack of adequate recruitment is blamed on the poor economic returns, the lack of established positions in the larger hospitals and health departments, and the lack of adequate training grants. The Canadian Association of Medical Bacteriologists believes that many jobs can be done only by medically qualified bacteriologists, but that if recruitment continues to be poor they will have to be filled by persons without proper qualifications. They recommend that each teaching hospital in Canada accredited for advanced graduate training in medicine or surgery and each large general hospital should have on its staff a medically qualified bacteriologist on a full-time basis. They recommend that such bacteriologists should enjoy the same income as other medical laboratory specialists and that adequate training grants should be established to allow attendance at formal university courses leading to a higher qualification in bacteriology.

DENMARK

Tuberculosis Morbidity.—Dr. E. Groth-Petersen (*Ugesk. læger*, March 20, 1958) compared the tuberculosis morbidity among persons over 15 who were tuberculin-positive with the morbidity among adults in the population as a whole in the period 1952 to 1955 inclusive. The tuberculosis morbidity per 100,000 in the first group fell from 44 to 36, whereas in the latter it fell from 41 to 21. The difference in favor of the latter was greatest in respect of young adults. The first group, it should be noted, were tuberculin-positive as a result of infection and not to BCG vaccination. Groth-Petersen concluded that fully one half of the adult population of Denmark is still tuberculin-positive as a result of infection.

Cerebral Abscess.—Dr. C. V. Fog (*Nord. med.*, April 3, 1958) studied a series of 114 patients with cerebral abscess and found that 33 were otogenic, 6 were rhinogenic, 28 were thoracogenic, 11 were craniotraumatic, and the remaining 36 were of some other origin. Supratentorial greatly outnumbered infratentorial abscesses. Those of thoracic origin were so severe that 21 of the 28 patients died. A classification hinging on the bacteriological findings showed that 11 of the 23 patients in whom Staphylococcus pyogenes var. aureus was found died, whereas there were only 6 deaths among the 24 for whom culture proved sterile. Of the 17 in whom streptococci were found 12 died. There were 65 deaths in all. Even with the use of an antibiotic a 25% mortality must be expected. A follow-up examination of the 49 survivors revealed that 31 were fit for work. Of the 18 remaining 13 had become epileptic. Total excision did not seem to give a higher mortality than more conservative measures.

Staphylococcic Infections in Hospital.—At a meeting of the Danish Society for Internal Medicine, reported in *Nordisk medicin* for April 17, several speakers stated that staphylococcic infections were a serious hazard on medical as well as surgical wards. On the medical side of the Blegdam Hospital between March, 1954, and the end of 1956 there were 55 such cases, the infection having been brought in from the outside in 14 cases and being nosocomial in 41. Of the 5 that were very serious, 3 were enteritic, and these patients successfully responded to erythromycin. The phage-type 80 organisms responsible for infections in Australia at the same time, gave rise to an outbreak of boils and abscesses in seven patients and one nurse in a 16-bed ward. Nearly all the victims of this type were elderly and debilitated women. The present high rate of staphylococcic infections may largely be due to a change in the composition of hospital patients who now are often old, debilitated, and just kept alive by modern methods of treatment. Systematic bacteriological examinations of the nurses in 8 surgical hospital units in Copenhagen showed that over 50% harbored Staphylococcus pyogenes var. aureus in the nose and that 86% of these were penicillin-resistant. About 67% of these nurses lost their staphylococci when on vacation. Another speaker remarked on the curious immunity to infections of the nose with staphylococci enjoyed by some nurses. His remedy for staphylococcic hospital infections was to discontinue the indiscriminate prophylactic use of antibiotics on a grand scale. He referred especially to an epidemic of measles in which 30% of the recipients of prophylactic treatment with penicillin developed secondary infections, whereas this was the case with only 15% of the patients not so treated. He also referred to the likelihood of the recipients of prolonged treatment with steroids to develop staphylococcic infections.

INDIA

Pathogenicity of Entamoeba Coli.—Kasliwal and Sogani (*Indian Journal of Medical Sciences*, vol. 12, February, 1958) stated that although it was first thought that of the intestinal protozoa only Entamoeba histolytica was pathogenic, doubts have been raised from time to time and evidence is now available to show that E. coli is capable of ingesting red blood cells both in culture and in the intestine. The authors observed 43 patients with colitis in whom no evidence of E. histolytica infection was found on repeated stool examination. The age of these patients varied between 8 and 70. They complained of abdominal pain, anorexia, diarrhea or constipation, and vomiting. The liver was palpable in 32. One had an amebic abscess from which 13 oz. of typical pus was aspirated. Microscopic examination of the pus showed Charcot-Leyden crystals, fatty acid crystals, and degenerated liver cells, but no protozoal growth was obtained on culture and no other organisms could be grown. The cecum was palpable and tender in 12 patients and the descending colon in 27.

Stools of all the patients showed E. coli infection. Other parasites associated with it were Giardia lamblia in four, Iodamoeba buetschlii in four, and Ankylostoma duodenale in one. Stool cultures were made from 25, and of these 15 showed pure E. coli growth. Sigmoidoscopy was performed on 14, of whom 10 showed a normal mucosa. One to three small ulcers with raised margins were seen in the rectosigmoid of the other four. Microscopic examination of scrapings from these ulcers showed trophozoites of E. coli in two. Most patients had mild to moderate anemia. Of the 43 patients, 9 left against medical advice and the rest received emetin followed by carbarsone or iodochlorhydroxyquin after a preliminary treatment with penicillin to overcome the secondary infection; 17 obtained complete relief and the rest had a varying degree of symptomatic relief. At the time of discharge only 8 of the 34 were passing cysts of E. coli in their stools. The colon was not tender in any patient after treatment. Before treatment, 15 of the 34 had an enlarged tender liver, but after treatment the liver was barely palpable and slightly tender in only 2 and palpable but not tender in 2. These patients thus showed the clinical findings of amebiasis and were greatly improved after antiamebic treatment, but repeated stool examinations were negative for E. histolytica while E. coli was found in all and also in scrapings from intestinal ulcers. This was considered strong circumstantial evidence that the latter is a pathogen.

Tuberculosis in the Army.—Pulmonary tuberculosis is the principal cause of separation from the Army, with injuries and psychiatric diseases following in second and third place. M. C. Sanyal (*Indian Journal of Tuberculosis*, vol. 4) collected data over a two-year period from hospitals where patients with pulmonary tuberculosis were admitted; from the annual health reports of the Chief Sanitary Commissioners, the Public Health Commissioners, and the Army; and from the results of mass miniature radiography in military hospitals—the records of 9,278 persons in all. Since 1900, the incidence of pulmonary tuberculosis in the Army declined from 3.7 per 1,000 in 1900 to 1.24 per 1,000 in 1949. The incidence was never high during this period although there were peaks coinciding with World Wars I and II. The fall was steady and slow and was more likely the result of a social trend than of any preventive measures. A study of age incidence showed a small rise up to the age group 40 to 45 years, then a slight fall, and the final rate was a little higher than in the age group of 18 to 20 years.

In Gurkhas and hill people there was a definite peak in the age group 30 to 35 years. This is to be expected in a population with relatively little contact with pulmonary tuberculosis and therefore little immunity to it. Meeting the disease for the first time in adolescence and early adult life, they have a much higher incidence than other adults in the Army who have been in contact with it since childhood. In the age group 18 to 20 years, the training period of recruits, there was no pulmonary tuberculosis among Gurkhas. Results of mass miniature radiography showed that among the naval personnel examined, of the total detected abnormalities, pulmonary tuberculosis comprised 52.9%. This incidence was 81.4% in trained Gurkha soldiers and 30.7% among untrained Gurkhas. The artillery and infantry (the two branches which involve heavy physical stress and strain) and Army medical personnel whose duties involve caring for tuberculous patients showed the highest incidence of this disease. A much higher incidence was observed among the married than among the unmarried men. The campaign against pulmonary tuberculosis at present provides mass miniature radiography of Gurkha recruits before acceptance and BCG vaccination of all susceptibles among Gurkhas. This is also extended to their family members. A follow-up of family contacts in a household where one member is suffering from this disease is also advised.

Effect of Hypothermia on Brain and Heart.—B. K. Anand and co-workers (*Indian Journal Medical Research*, vol. 46, January, 1958) stated that although hypothermia has offered new prospects in the treatment of congenital heart disease, cerebral vascular tumors, and aneurysms, its use is attended by certain hazards. It induces serious cardiac arrhythmias and irreversible changes in the nervous system, especially in the heart regulating mechanism and the respiratory and cardiovascular centers. These complications have been variously assigned to conflicting mechanisms. The authors estimated the acetylcholine and glutathione content of the

heart and brains of 6 normal and 14 hypothermic dogs. The normal averages of acetylcholine and glutathione content of the heart, hypothalamus, and frontal and temporal lobes of the brain were worked out from the values obtained in the control animals. The acetylcholine level of the heart was lower than that of the nervous tissue and the hypothalamic region contained an appreciably higher level than the frontal and temporal lobes. The glutathione content of the heart was also lower than that of the nervous tissue but the hypothalamus contained about the same amount as the frontal and temporal lobes.

An average fall of 14.5 C below the average body temperature was obtained by hypothermia. Hypothermia of this degree decreased the amounts of both acetylcholine and glutathione in the heart and the hypothalamic and frontal regions of the brain, but it increased both the acetylcholine and glutathione content of the temporal lobes containing the hippocampus. As the periamygdaloid region containing the hippocampus is related to the maintenance of body temperature, this region may be becoming hyperactive to counteract the hypothermia and maintain the normal surface and visceral temperature. The increase in the acetylcholine and glutathione is a result of the increased metabolic activity. In the heart and nervous tissue, the cellular metabolism is diminished during hypothermia and this is reflected in the loss of the two chemicals studied here. The authors suggested that it may be profitable to give adequate doses of acetylcholine and glutathione during hypothermia to prevent abnormal rhythms in the heart and failure of the vital nervous centers. This is especially important in the recovery phase when the temperature starts rising, as at this time metabolism in the tissues is increased and there is likelihood of the development of anoxemia.

NEW ZEALAND

X-ray Hazards.—The New Zealand branch of the College of Radiologists of Australasia in a report on radiation dangers stated that the risk of danger from a diagnostic x-ray examination by a properly trained operator is nonexistent, but it warns that too many reexaminations in any anatomical site are at present being undertaken without critical appraisal of the need for such examination. Much unnecessary apprehension has been created by public statements of the risks, not counterbalanced by any consideration of the value, of medical x-rays. There is some ground for supposing that unborn children are more sensitive to x-rays than adults, but so far exhaustive research has not proved that x-ray examination of the mother involves a significant risk for the child. Against this possibility must be balanced the certain risk to mother and child if x-ray examination is omitted when it would have been helpful. In diagnostic x-ray examination by a skilled operator the dose is so small that the risk of any genetic effect is remote. By continued improvement of the already very safe conditions under which x-ray examinations are made scientists are reducing such risks to an even lower level, and, in some cases, eliminating them completely. The college believes, however, that routine roentgenography of the chest in persons under 16 years of age is not justified. Reexamination of patients with known tuberculosis should be preceded by a clinical examination to determine, among other things, the necessity for roentgenographic reexamination. Any program, such as national mass surveys, and routine examination of specific groups, such as nurses, should be the subject of periodic review to determine whether continuance or modification is justified by the results being obtained.

Endocrine Homotransplants.—Woodruff and Sparrow who previously showed that rats injected subcutaneously with homologous spleen cells in suitable dosage on the day they are born are, when they grow up, almost completely tolerant of skin homografts from the same donor, now report the results of some experiments designed to determine whether tolerance induced in this way might be extended to homografts of other tissues, especially of thyroid and adrenal tissues (*Quart. J. Exper. Physiol.* **43**:91, 1958). Litters of newborn Wistar rats were subdivided into four pairs of animals of like sex. One member of each pair received a subcutaneous injection of a suspension of spleen cells from an adult of the same sex, and the other member served as a control. When they were 12 weeks old, each injected animal received a homograft of either thyroid or adrenal tissue from the original cell donor and each control animal a homograft of thyroid or adrenal from a stock rat of the same sex.

The technique for assessing the viability of thyroidal grafts consisted of measuring the uptake and release of I^{131} from the thyroid grafts. These measurements provided a useful means of assessing the amount of surviving thyroid tissue and its functional activity. Homografts of thyroid tissue placed alongside the femoral vessels in thyroidectomized rats, injected at birth with spleen cells from the same donor, were as a rule indistinguishable from autografts both in their capacity to take up I^{131} and in their histological structure, whereas homografts in thyroidectomized but otherwise untreated rats were usually destroyed within six weeks. Homografts of whole adrenal glands sutured to the ovaries of adrenalectomized recipients which were injected at birth with donor spleen cells also behaved like autografts. Homotransplants in adrenalectomized control hosts were sometimes destroyed in a few weeks, but sometimes survived for months, though they usually showed evidence sooner or later of replacement of cortical tissue by connective tissue.

The authors concluded that observations on the uptake and release of I^{131} provided a reliable means of assessing the behavior of thyroid grafts and in particular the amount of surviving thyroid tissue and its level of functional activity. Subcutaneous injection of homologous spleen cells at birth appeared normally to result in a high degree of tolerance to thyroid tissue from the same donor, as well as in a tolerance to adrenal cortical tissue. The evidence, however, was not quite as conclusive in the latter, because adrenal homografts to the ovary sometimes survived for several months even in control hosts. The discovery that tolerance induced by spleen cells is not confined to skin homografts but extends also to homografts of endocrine tissue provides strong evidence that all the transplantation antigens present in the cells that constitute these tissues are present in the cells of the spleen and is consistent with the view that the antigens concerned in transplantation immunity are common to all the nucleated cells of an individual.

Immunological Problem of Pregnancy.—Three factors have been suggested to account for the fact that the mammalian fetus, which differs from the mother in its genetic constitution, escapes the usual fate of homotransplants and continues to survive and develop in the mother throughout the period of gestation. These are (1) the anatomic separation of the fetus from the mother, (2) the antigenic immaturity of the fetus, and (3) the immunological inertness of the mother. Prof. M. F. A. Woodruff (*Proc. Roy. Soc. London. Ser. B* **148**:68, 1957) reported the results of some experiments, carried out at the Otago Medical School, designed to assess the importance of the first factor.

In one series of experiments 40 pairs of rats were mated. In each case the female was a virgin Wistar rat about 4 months old and the male was a black-and-white hooded rat of about the same age. Four or five weeks prior to mating 18 of the females had received a split-skin graft from the male with which it was subsequently mated, and these grafts survived as expected for about 12 days. This procedure had been shown previously to evoke a high degree of immunity to subsequent grafts from the same donor. The recipients are referred to as "immunized," and the animals that did not have skin grafts served as controls. Mating was performed during estrus, and the male was removed after 24 hours. Fifteen days after mating, if palpation showed that the female was pregnant, the upper portion of the left horn of the uterus, including the highest fetus, was removed aseptically, with the animal under ether anesthesia, through a dorsal incision. The remaining fetuses and the ovaries were interfered with as little as possible. The two hindquarters of the fetus were dissected free and grafted intramuscularly to the mother, one graft being placed in each flank. The left graft, with adjacent host tissue, was removed for histological examination after 6 days and the right graft after 14 days. The young appeared healthy at birth and developed normally. There was no significant difference in the average number per litter from immunized and control mothers. The histological sections of the hindquarters grafted to the control mothers showed recognizable fetal tissue with numerous mitotic figures and no evidence in general of host reaction, whereas in the immunized mothers there was no recognizable fetal tissue in the graft and no mitotic figures were found. There were areas of necrosis and hemorrhage, surrounded by young connective tissue containing numerous engorged blood vessels packed with red blood cells and dead leukocytes. The histological findings thus closely resembled those seen in grafts of adult tissue in previously immunized animals.

The second series of experiments was similar in principle to the first except that rabbits were used instead of rats. The results also closely resembled those of the first experiment. The analogy between the results is of interest because in the rat the passage of antibodies from mother to fetus, if it occurs at all, is on a limited scale, while in the rabbit the antibodies pass readily from mother to fetus via the splanchnopleure of the yolk sac. The behavior of the fetal tissue grafts in the control animals in both experiments provided strong evidence that the mother does not become effectively immunized against fetal tissues during normal pregnancy. The behavior of the fetal tissue grafts in the immunized animals showed, on the other hand, that females receiving a skin graft from the male with which they are subsequently mated are effectively immunized against grafts from fetuses resulting from the union. This is not surprising, since the fetus derives from the father many genes foreign to the mother and is in consequence likely to possess, at least after a certain stage of development, tissue antigens not possessed by the mother. It is significant, however, that even when a high degree of immunity to fetal tissues is produced experimentally in this way, conception occurs as readily as in nonimmunized animals and pregnancy runs its normal course. These findings suggest that the decisive factor to overcome the immunological hazards of pregnancy is the anatomical separation of mother and fetus. The crucial feature of this separation is that it normally prevents maternal cells from gaining access to the fetus.

NORWAY

Paralysis Agitans.—Hörsdal (*Tidsskrift for den Norske lægeforening*, April 1, 1958) used benztropine to treat 20 patients with paralysis agitans. By mistake, 2 mg. were given 3 times a day in one case for 3 days, after which drowsiness and pareses of

the arms and legs led to the drug being withheld. With a smaller dosage (1 mg. daily, raised in 2 to 3 weeks to 5 mg. daily) encouraging results were obtained. All the patients noted a lessening of rigidity and most of them less tremor. The gait became more natural and the facial expression more relaxed. In most patients sleep was improved. Several patients noticed slight dryness of the mouth, and two had slight blurring of vision. With the exception of the victim of overdosage, all the patients were anxious to continue this treatment, which was, however, hampered by its high cost.

Cancer from Medicinal Use of Arsenic.—Dambolt and Foss (*Tidsskrift for den Norske lægeforening*, April 1, 1958) condemned the vogue for prescribing arsenic for a great variety of ailments. They have treated four patients whose cancer followed the prolonged administration of arsenic. The lungs were invaded in two of these, and keratoses due to arsenic were observed in three other patients after prolonged arsenic medication. The authors sent a questionnaire to 90 patients who had survived an operation for lung cancer. Of the 74 who answered 12 had had a course of arsenic treatment much earlier in life. To learn the extent to which such courses are popular, 248 skin patients over the age of 20 were asked if they had ever had such a course, and it was found that 19% had. In the last 27 years an average of 50 kg. of arsenic have been sold yearly by druggists in Norway. These sales have declined somewhat in recent years. The authors challenge the basis on which arsenic has been prescribed since cases of carcinoma due to arsenic were first reported in 1887. Arsenic may have fallen into disrepute as a general tonic and as a treatment for acne, eczema, and alopecia, but opinions are still divided over its value in treating psoriasis. Although its use is still justifiable in some cases caution is needed if the complaint is chronic and particularly if the patient is young. In treating pityriasis rubra pilaris arsenic may be beneficial and even indispensable if the patient is middle-aged or elderly. The same may be said of Boeck's sarcoid, but in general arsenic should be prescribed with great parsimony and circumspection.

Sedimentation Rate and Serum Cholesterol.—At the Kroghstötten hospital in Oslo, several patients were found to have a high sedimentation rate of unknown origin associated with a pathologically high total serum cholesterol concentration. Dr. Jarle Ofstad (*Nord. med.*, April 17, 1958) reviewed the records of 19 patients with primary hypercholesterolemic xanthomatosis with special reference to their sedimentation rates and found that the rate rose with the rise of the concentrations of total cholesterol, free cholesterol, phospholipid and, in some degree, beta-globulin. Although his series was too small to warrant any conclusion as to a causal relationship, they make such a relationship appear likely.

Blood Pressure.—The late Professor H. Rasmussen devised an ambitious plan for an investigation of the blood pressure of the inhabitants of Bergen, in connection with a more or less compulsory mass roentgenography survey of its population in 1950-1951. The ages, heights, and weights of the subjects were also recorded. Fröystein Wedervang analyzed this series of about 70,000 observations for his doctor's thesis. He concluded that the blood pressure rises with age, being lower among young females than males of the same age but the rise with growing years is greater for females than for males till they run level, and ultimately the pressure is higher in the female. Within each age group there are wide variations in the range of pressure measurements, and this range grows with age. It is commonly assumed that overweight sends the blood pressure up, but if it does so, the figures are not impressive, with a rise of only 2 or 3 mm. Hg for every 10 kg. of body weight gained. The height-weight measurements showed among other things that, with a given height, there was a marked mean rise of weight with increasing years, overweight being conspicuous for women between the ages of 45 and 65.

SWITZERLAND

Psychomotor Aspects in Children with Behavior Disturbances.—Dr. H. Feldmann (*Médecine et Hygienè* **16**:165, 1958) reported that changes in the personality and in behavior in children necessitates a search for causative factors. In all members of a series of 40 such children aged 7 to 17 years the author found significant emotional conflicts. Nine of the children showed disturbances in motor function, accompanied by oral fixation in 3, anal regression in 3, and nonresolution of the Oedipus complex in 2; 12 had significant ideomotor dyspraxia with dyskinesia; and on the affective plane he found poor identity in 4, anal regression in 3, and an abnormal Oedipus fixation in 3; 12 others had psychomotor instability, associated with reactional aggressivity in 7 and significant primary anxiety in 4; and 7 showed no motor disorders but had severe ego and affective disorders representing principally a reaction to a disturbing environment. For want of time and funds the children were not subjected to psychotherapy but merely to psychomotor reeducation, by means of rhythmic gymnastics, and to medical treatment. They made a progressive and gratifying adjustment to the external world. Their parents were advised as to the method of education to be adopted in each case. The

speaker concluded that affectivity can develop normally only if the motoricity also develops in the same way.

TUNISIA

Radioactive Iodine and the Human Fetus.—Although among the contraindications to the use of radioactive iodine (I^{131}), pregnancy is one of the most absolute, it may be possible under some circumstances that the presence of pregnancy is not recognized and I^{131} is given to a pregnant woman with toxic diffuse goiter. Dr. G. Valensi (*Tunisie méd.* 36:69, 1958) reported such a case in a 30-year-old woman who denied being pregnant. The results of the treatment were excellent. All the toxic symptoms improved rapidly, and the exophthalmos receded markedly. The patient later reported a delay in menstruation. Her pregnancy took a normal course, and a premature infant was delivered alive in the eighth month of gestation. It weighed 2,850 Gm. (6.3 lb.), but it showed extensive malformations. The skin was thickly infiltrated as in patients with myxedema; the head in relation to the body was too large; and a pronounced exophthalmos was present. The child died half an hour after birth. It may be assumed that the thyroid of the fetus had taken up a large dose of I^{131}, in the fourth week of intrauterine life, which completely destroyed the thyroid. The absence of the thyroid hormone caused hypersecretion of the thyroid-stimulating hormone of the pituitary, thus producing the infiltration of the skin due to absence of thyroid and pronounced exophthalmos due to hypersecretion of thyroid-stimulating hormone.

UNITED KINGDOM

Poliomyelitis Vaccine.—Poliomyelitis vaccine has become a heated political issue. In a speech the Minister of Health before the House of Commons said that he proposed to import an adequate amount of Salk vaccine from the United States and Canada, without submitting it to any special tests in the United Kingdom, to supplement supplies from the two British companies that are producing the vaccine. There are three standards of safety so far as poliomyelitis vaccine is concerned. The safest is that produced in England; next comes the vaccine produced in the United States and Canada and submitted to additional tests in England; and finally comes the vaccine produced in the United States and Canada that satisfied the tests applied in these two countries but had not been tested in England. In view of the necessity for inoculating the priority classes enumerated by his experts—children under 15 and expectant mothers—the Minister, on the advice of his experts and as an emergency measure, was arranging for Salk vaccine produced in the United States and Canada to be used without additional testing. What worried many physicians was the vacillation the Ministry of Health has shown in this matter in the last two years and the effect this may have on mothers. In the first instance, the Minister declared that under no circumstances would he allow American-produced Salk vaccine to be used in this country. When this source proved hopelessly inadequate, he suddenly changed his policy and said that a limited amount of American vaccine would be imported on condition that it was submitted to stringent testing before use. Now he has again changed his policy and said that the vaccine, which up to a week or so ago, was not safe for British children can be used. The fact that he still contends that such vaccine is less safe than that being produced in this country has done nothing to allay public fears.

Duration of Night Feeding in Infancy.—In Middlesex, where demand feeding is encouraged by physicians and child welfare clinics, Janet Campbell (*Lancet* 1:877, 1958) attempted to determine how long an infant must be fed at night. No significant difference was observed between bottle-fed and breast-fed babies or between those born at home or in an institution. The important factor was weight at birth. Thus, of the 55 babies whose weight was less than 6.5 lb. (2.95 kg.) at birth, only 9% had never had a night feeding, compared with 52% of the 63 who weighed more than 8 lb. (3.60 kg.) at birth. By the age of 3 months these differences had disappeared, and by this age 91% of those with a birth-weight of less than 6.5 lb. (2.95 kg.) and 89% of those weighing more than 8 lb. (3.60 kg.) at birth had ceased their night feedings. In most cases night feeding stopped fairly suddenly. The usual story was that the baby slept through the night two or three times one week, and then the next week or the one after he no longer demanded a night feeding.

Declining Vaccination Rate.—Vaccination after birth ceased to be compulsory in Great Britain with the passing of the National Health Act in 1948. As a result only slightly more than 33% of infants are now vaccinated within the first year of life. Parents are anxious to immunize their children against diphtheria and poliomyelitis, which catch the public eye, but the threat of smallpox is not regarded seriously by parents. In Scotland the smallpox vaccination rate in the cites and towns varies from 82% to as low as 14%, in spite of propaganda drives. An inquiry showed that the most effective means of getting parents to have their children vaccinated was persuasion by the family physician and health visitor. The public are immune to overt propaganda in the form of official announcements, posters, leaflets, and the like.

Iodized Salt.—Selwyn Taylor (*Lancet* 1:751, 1958) made a plea for the use of iodized salt. The cost to the country annually of not iodizing salt as measured in terms of demands made on the medical services and loss of working time are enormous. The Medical Research Council in 1944 and again in 1948 recommended iodizing salt, as practiced in many other countries, but as yet no official action has been taken.

Sulfonamide Hematuria in Children.—In the 10 years since 1948, 29 children were treated in the medical wards of the Royal Hospital for Sick Children, Glasgow, for hematuria associated with taking sulfonamides, according to G. C. Arneil (*Lancet* 1:826, 1958). Although all subsequently recovered, anuria, hypertension, encephalopathy, and uremia were encountered in some of the patients. All but two had been given a preparation containing sulfamerazine, and in 13 of these the dosage used approximated that recommended by the manufacturer. There was no evidence that the fluid intake of these children was restricted. Despite the fact that, under ideal conditions, with a dose every 12 hours and copious fluid and alkali administration, the drug seldom produces hematuria, the overriding consideration here is that in practice this drug may cause hematuria, azotemia, and hypertension in children when given at a dosage level in frequent use. To justify giving a drug potentially toxic in therapeutic doses one must show that it has significant advantages over other preparations. Sulfamerazine appears to have no such advantages.

Hypnotism in General Practice.—According to A. A. Mason in a symposium on hypnotism reported in *The Practitioner* (**180**:597, 1958) hypnosis can be practiced by all, as it is easy to learn and requires no special ability or power. About 85% of the population can be hypnotized and hypnosis is an ideal anesthetic, but the deep trance necessary for this can only be produced in about 20% of all patients. On the other hand, 50% of patients may thus obtain sufficient analgesia for such minor operations as dental fillings, reduction of fractures and dislocations, and painful dressings. Hypnotism is especially valuable as an analgesic in obstetrics, giving pain relief in a high proportion of patients without interfering with labor or depressing the fetal respiratory center. Direct hypnotic suggestion aimed at symptom removal is often useful in such psychosomatic disorders as chronic skin diseases, and Mason reported a 50% recovery rate in 200 patients with previously chronic cases. Habits and such mild compulsions as nail-biting, cigarette smoking, overeating, and hiccups responded favorably. Hypnosis can be of more use to the general practitioner than to anyone except the anesthetist.

C. A. H. Watts was not so certain about this and had given up using hypnosis in his practice. He first asked why, if hypnosis is so safe and effective, it had not been widely used by the profession as a whole. After all, many conditions said to respond to hypnotism, such as asthma, enuresis, and smoking are troublesome to both the consultant and the general practitioner. He had found that the patient who will agree to this type of treatment is the exception and not the rule. Even more important than the right type of patient, in his opinion, is the right type of physician. Few doctors can stare confidently into their patients' eyes using the formula of the hypnotist. The family doctor who practices hypnotism is apt to become labelled, and this is undesirable as many people are fearful of the procedure and the physician who uses it. Frank hysteria is the ideal indication for hypnosis, but it is rarely seen in general practice, and there are usually easier alternative methods of treatment.

Alopecia due to Dextran.—The occurrence of alopecia in 8 of 15 patients treated with dextran sulfate, when the total dose was 90,000 units or more, was reported by G. R. Tudhope and co-workers (*Brit. M. J.* 1:1034, 1958). In six of these patients there was almost complete loss of scalp hair. Loss of pubic, axillary, and facial hair also occurred in three. Three of those who suffered severe loss of scalp hair were women, one of whom had complete loss of axillary and pubic hair and partial loss of her eyebrows. In all patients the hair ultimately returned to normal. The mechanism by which dextran produces its effect on hair growth is unknown, but it is suggested that it may interfere with the metabolism of the naturally occurring sulfated polysaccharides or the sulfur-containing amino acids. Diarrhea and depression of the platelet count were also encountered. This combination of toxic effects (alopecia, diarrhea, thrombocytopenia, and anorexia) is similar to the effects of whole-body irradiation and of exposure to nitrogen mustards, colchicine, and other antimitotic substances. The production of alopecia by dextran may be only one aspect of a more general and fundamental action of the drug. In spite of the advantage of good control of clotting time with infrequent injections, it is clear that, when dextran is given in a total dose of more than 90,000 units, toxicity occurs too often. No toxic effects were observed when the total dose was less than 40,000 units. Thus, 5,000 units of dextran given intravenously every 8 hours for 24 to 48 hours appears suitable as an alternative to heparin to cover the period until an orally given anticoagulant becomes effective.

MISCELLANY

CLINICAL APPLICATION OF RADIOACTIVE ISOTOPES

Radium and x-rays have been used for 60 years as a routine part of radiologic practice. The newer radioisotopes differ in no essential way except that they are artificially produced in a nuclear reactor. With proper precautions their use should be as safe, or safer.

As an indication of the popularity of isotopes, the Oak Ridge National Laboratory has dispensed over 100,000 curies of isotopes—equivalent to 200 pounds of radium (less than 3 pounds of actual radium is available in the world today).

Physical Aspects

Radioactivity implies atomic nuclear change that results in the emission of rays from the atom. A sample of a given element placed for a suitably short time in a nuclear reactor becomes transformed usually to a radioactive form of the same element. This is usually brought about by a shift in the number and relationship of the neutrons and protons in the orbit of the atom.

For example, a piece of gold foil the size of a postage stamp left for one week in a nuclear reactor becomes the equivalent, in radioactivity, of one gram of radium. In other instances one element is transformed into another. In practice, radioactive phosphorus (P^{32}) actually is made from elemental sulfur. In others the needed isotope, like radioiodine (I^{131}), is formed as an essential part of the manufacture of the atomic bomb and only requires isolation and processing.

It is essential to bear in mind that a constant fraction of the atoms of any radioisotope disintegrate or explode at a constant rate in a given period of time. If, for instance, we have one hundred atoms present at the start and find that one day later there are only fifty, we can say that its "half-life" is one day and can predict with almost absolute accuracy that at the end of two days there will be only twenty-five.

Let us then examine the different types of radiation. For purposes of general classification there are two main types: corpuseular and electromagnetic. The corpuscular types are actual particles of matter having measurable mass and moving at moderate rates of speed. They have the capacity of poor tissue penetration. Electrons (protons and neutrons), alpha particles (radium), and beta particles (radium, P^{32}, and I^{131}) are examples of the corpuscular types of radiation. Electromagnetic types differ in that they have no mass, no weight, and no charge. They move at the speed of light and have wave length and frequency. Examples of electromagnetic types of radiation would include light and have wave length and frequency. Examples of electromagnetic types of radiation would include light, radio and television, x-rays and gamma rays (I^{131}, radium, x-rays).

Clinical Applications—Diagnosis

Radioactive isotopes have made available an indispensable tool in basic scientific research as well as in the field of clinical medicine. Radioactive gold (Au^{198}) and yttrium (Y^{90}) have been used with some success in decreasing pleural effusions due to carcinoma. Radioactive phosphorus (P^{32}) is being used to treat polycythemia vera, certain leukemias and to locate intraorbital tumors. Radioactive cobalt (Co^{60}) is used to label viatmin B_{12} for a test to detect the presence or absence of the intrinsic factor in cases suspected of having pernicious anemia. Radioactive iodine (I^{131}) has found application in the diagnosis and treatment of certain thyroid disorders and in the treatment of certain types of euthyroid heart disease.

In the field of thyroid disease I^{131} is a very versatile and useful isotope. While most diseases of the thyroid can be diagnosed by history and physical examination, together with a minimal amount of laboratory work including a basal metabolic rate and serum cholesterol, there is a significant group that still offers diagnostic difficulty. The thyroid gland may be considered as a continuously running production line. Iodine is trapped, taken into the thyroid cells, utilized to form hormonal compounds (diiodotyrosine, triiodothyronine, tetraiodotyrosine), released and transported to the tissue cells. The basal metabolic rate measures the degree of cellular stimulation by measuring the metabolic rate of the cell. The radioiodine uptake measures the rate of endocrine activity of the thyroid by measuring either the degree of iodine uptake into the gland or the rate of iodine turnover, clearance, and utilization by the gland. The protein-bound iodine measures the amount of iodine that is bound to thyroglobulin as it is being transported from the gland to the tissue cells.

The technic of a radioactive iodine uptake study is quite simple. A tracer dose of radioiodine containing from 10 to 50 microcurie is given orally, and monitoring of the thyroid area at the end of twenty-four hours is accomplished by the use of a scintillation counter. Standards are likewise counted and calculations are made, based on the amount of radioactivity given. The percent uptake of the radioactive material by the thyroid is determined

Condensation of an article by Ben D. Hall, M.D., presented before the Tennessee Regional Meeting, American College of Physicians, Paris Landing, Tenn., Oct. 19, 1957, and published in the *Journal of the Tennessee State Medical Association*, April, 1958.

with a standard formula. In general, uptakes from 0 to 15% are indicative of hypothyroidism. Uptakes from 15 to 45% indicated euthyroidism. Uptake values between 45 and 50% are considered borderline, and uptakes above 50% indicate hyperthyroidism. . . .

Previous treatment with inorganic iodides such as Lugol's solution or potassium iodides will result in a falsely low value. This is likewise true for the organically bound iodine utilized in intravenous pyelograms, myelograms, cholecytograms, etc. The prior use of goitrogenic drugs, such as propylthiouracil, will likewise invalidate the accuracy of the test unless the drug has been discontinued for a period of time prior to the test.

In cases where the iodine uptake is borderline normal, other tests may be desirable. In certain cases a thyroid clearance test may be helpful. This measures the rate of clearance of the iodine from the blood by the thyroid. The radioiodine is given intravenously and periodic measurements of the thyroid gland and the plasma are made at specific intervals. Results are expressed as milliliters of plasma per hour cleared of radioiodine by the thyroid gland.

The chemical measurement of the protein-bound iodine is highly technical and not widely available. However, after a suitably high tracer dose of I^{131} is given, that portion of iodine bound to protein can be detected in a well counter and the percentage of organically bound iodine can be determined. This is done either by precipitating the protein fraction or by removing the inorganic portion by absorption onto a resin column. This gives the protein-bound iodine conversion ratio which is of diagnostic value in some cases where the iodine uptake is in the borderline range.

Another test of value is the thyroid suppression test. In certain instances where the original uptake value is of borderline elevation, the patient is given large doses of desiccated thyroid or triiodothyronine for 10 to 14 days to suppress thyroid function. The 24 hour uptake is then repeated. If the gland is truly overactive no significant reduction in uptake is observed. If the gland is basically euthyroid the second uptake will be significantly lower than the first.

In addition to uptake studies the gland may be scanned for the study of thyroid nodules. This may be done by the use of a handheld probe or by the use of a mechanical device which may actually record a scintogram of the gland. In 1940, Hamilton, Soley, and Eichorn, using radioautographic studies of thyroid tissue slices, found that cancerous tissues retain practically no radioiodine whereas normal thyroid tissue concentrated large amounts of the isotope. Cope, Rawson, and McArthur, and several others working independently reported that benign hyperplastic nodules concentrated more radioactive iodine than normal tissue. . . . In general it may be stated that malignant nodules do not pick up radioiodine and will be "cold" as far as selective counting is concerned. Metabolically inactive thyroid tissue, due to any cause, likewise will be "cold" (hemorrhagic cyst, areas of thyroiditis, calcification, fibrosis, etc.). Hyperplastic nodules will concentrate more radioiodine than will contiguous tissue and can be identified accurately. This technic has limited application in the therapy of nontoxic nodular goiter by the use of thyroid feeding with large doses of desiccated thyroid in an attempt to suppress pituitary thyroid-stimulating hormone. . . .

Treatment

Radioiodine treatment is indicated in the following circumstances: (1) uncomplicated hyperthyroidism over age 40; (2) recurrent or persistent postoperative toxicity; (3) toxicity in poor surgical risk patients; (4) idiosyncrasy to antithyroid drugs; (5) refusal to accept surgery; and (6) severe or progressive exophthalmos.

Treatment with radioactive iodine may be considered contraindicated in the following circumstances: (1) uncomplicated hyperthyroidism under age 40; (2) toxicity in children; (3) pregnancy or lactation; and (4) large toxic nodular goiters.

The advantages of oral treatment with radioactive iodine are obvious. No hospitalization is necessary. There is no operative mortality, discomfort or scar, and there is no danger to the recurrent laryngeal nerve or parathyroid glands. Inasmuch as treatment may be given on an outpatient basis, there is minimal loss of time from work and minimal expense.

Treatment is given orally on a fasting stomach. The dosage is designed to deliver to the gland between 100 and 140 microcurie per gram of gland, or to deliver between 5,000 and 10,000 roentgen equivalent physical (rep). There are as many methods of estimating dosage as there are groups giving therapy. In general the results reported are similar—85% are euthyroid after one or more treatments. The incidence of post-treatment hypothyroidism varies between 4 and 18 percent. As a general rule those who tend to give low initial doses will have a higher incidence of retreatments but will have a lower incidence of post-treatment hypothyroidism. The most important factor in determining the dose is clinical judgment. This includes factors such as the size of the gland, the presence or absence of nodules, the clinical degree of toxicity, the percent uptake at the end of twenty-four hours, the age of the patient, and the presence of associated but related disease.

We have utilized the following modified Quimby formula for calculation of the dosage designed to deliver from 5,000 to 10,000 rep:

I^{131} to deliver 1,000 rep = weight of gland $\times$ 0.0555 $\div$ the percentage uptake times the biologic half-life.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Problem of Chronic Pneumonia. K. G. Nikulin. Klin. med. **35**:46-50 (Dec.) 1957 (In Russian) [Moscow].

Chronic pneumonia is a poorly defined but a rather frequent entity. It is commonly regarded as a manifestation of pneumosclerosis. The author insists that chronic pneumonia must be regarded as the primary and pathogenetic basis of pneumosclerosis, bronchiectasis, and pulmonary suppuration. Chronic pneumonia can be primary or secondary—the result of an acute pneumonia. It runs a protracted, undulant course with subfebrile temperature and sometimes without physical manifestations. The clinical picture becomes manifest with the development of bronchiectasis or of suppuration. Chronic pneumonia is resistant to antibiotics and to sulfanilamides. Its treatment, therefore, must be directed to the improvement of the general health, repeated blood transfusions, and vitamin administration. Chronic pneumonia complicated by bronchiectasis or suppuration must be treated surgically.

Comparative Study of Treatment with Hormones, Salicylates, and Phenylbutazone on the Basis of 631 Cases of Acute Rheumatic Fever Observed in Four Years (497 in Children). J. Chevallier. Rev. rhumat. **25**:1-17 (Jan.) 1958 (In French) [Paris].

The records of 631 patients with acute rheumatic fever treated during the period from 1953 to 1956 in 13 hospital services were reviewed and compared in relation to the 3 forms of treatment received. Sodium salicylate and aspirin were identical in their effect, lowering the erythrocyte sedimentation rate to a normal level within 5 or 6 weeks. Similarly, equivalent doses of the various hormones (corticotropin, cortisone, hydrocortisone, and deltacortisone) produced identical effects. The lowering of the erythrocyte sedimentation rate took place more rapidly in patients receiving the hormones than in those receiving salicylates (2 to 3 weeks instead of 5 or 6), but it was often accompanied by a transient hypofibrinemia. Phenylbutazone, the third form of treatment, had only a slow and incomplete effect on the erythrocyte sedimentation rate. The rebound of the rate, which is habitual after hormone treatment and which occurs fairly often after the administration of salicylates, seems to be rare in patients who have been treated with phenylbutazone. Leukocytosis returns to normal in 3 weeks under treatment with salicylates or phenylbutazone, but in patients receiving hormones this effect is produced more slowly. The course of the heart murmurs in the various therapeutic groups suggests that hormone treatment is superior to treatment with salicylates, but the number of patients is too small and the follow-up is too short for any definite statement to this effect. The effect of phenylbutazone on rheumatic carditis is an important finding, because it is in contrast to its mediocre effect on the erythrocyte sedimentation rate. Each of the 3 forms of treatment gives rise to certain complications, the most severe of which are occasional psychic disturbances in patients receiving cortisone or cortisone derivatives and hemorrhages of various kinds in patients receiving phenylbutazone.

Hormone administration, on the basis of this study, is regarded as the best treatment now available and the one that is the easiest to manage, especially when deltacortisone is used: it has the widest margin of safety between a useful and a toxic dose. Phenylbutazone seems to produce equally brilliant results, but complications are frequent and sometimes serious. Aspirin is apparently less effective so far as carditis is concerned; in addition, the fact that it has to be given in large doses, to the limit of tolerance, makes its use inconvenient.

Sarcoidosis and Tuberculosis. I. Ståhle. Nord. med. **59**:302-303 (Feb. 20) 1958 (In Swedish) [Stockholm].

Sarcoidosis and tuberculosis can occur in different combinations: 1. Tuberculosis, usually grave, develops slowly after primary sarcoidosis. 2. After a symptom-free period that follows an apparently healed tuberculous lymph-node or parenchyma process, a typical sarcoidosis develops without signs of activity of the tuberculous changes. 3. An active pulmonary tuberculosis passes directly into sarcoidosis with disappearance of the positive tuberculin reaction. Two cases of type 3, which is rare, are presented. In both cases the disease began

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as pulmonary tuberculosis, with positive tuberculin reaction and tubercle bacilli demonstrated in the sputum. In the first case unilateral pulmonary sarcoidosis gradually developed, with negative Mantoux reaction, after an interval with weakened positive tuberculin reaction and, simultaneously, bacteriologically established tubercle bacilli and histologically certain diagnosis of sarcoidosis. Microscopic examination of resected, formerly tuberculous segments showed only typical sarcoid structures. In the second case cutaneous sarcoidosis developed together with bilateral pulmonary sarcoidosis. The changes showed good regression on treatment with vitamin D (Fortedol). This treatment should be given in hospital with close control of the renal function. It is considered likely that long-term antituberculosis treatment, especially with isoniazid, may induce a change in the tubercle bacilli with subsequent development of sarcoidosis. Bronchoscopy with biopsy seems to be indicated in sarcoidosis.

Environmental Penicillin and Penicillin-Resistant Staphylococcus Aureus. J. C. Gould. Lancet 1:489-493 (March 8) 1958 [London].

The proportion of penicillin-resistant strains of Staphylococcus aureus is increasing in hospitals among carriers who are not receiving penicillin. This is usually explained by postulating a free interchange of organisms between the treated patients and these carriers, but this presupposes that the penicillin-resistant organisms have the power to replace the naturally occurring penicillin-sensitive carrier strains. So far there is no satisfactory evidence that this happens. Further, if mutation takes place in each patient under treatment, a much greater variety of phage types of penicillin-resistant staphylococci would be expected to occur in hospitals, whereas it is usual for only a few strains to be present in each hospital. Also, patients infected with penicillin-sensitive strains before treatment would be expected to yield penicillin-resistant strains of the same type after treatment. In fact, most patients who are investigated show the penicillin-resistant strains to be of different type from the sensitive strains originally present. Another possible explanation of the rapid colonization among carriers in hospital is that these persons receive in their noses enough penicillin, inhaled with air and dust and transferred from their hands and fingers, to maintain a nasal concentration of penicillin inhibitory to sensitive staphylococci. Evidence for this hypothesis was sought by testing the environment in a hospital for free penicillin and comparing the results with those found in a factory handling penicillin.

The hospital examined was a large general hospital with about 900 physicians and nurses. Permanent nasal carriers comprised 53% of the staff, and the proportion of these carriers harboring penicillin-resistant strains exceeded 90%. The factory examined handled penicillin from bulk and dispensed it in various forms. The amount of penicillin recovered in different parts of the hospital varied considerably but was greatest nearest those rooms where penicillin was being handled or therapeutically administered. Leakage from the phial during puncturing, clearing of air bubbles and froth from syringe and needles, and spraying when washing out the syringe commonly takes place during the process of injecting a patient. Air may be contaminated in 2 ways: directly, by droplets atomized from syringes and the like, and indirectly, by the raising of dried spilt penicillin as dust. The hospital environment can, therefore, readily acquire penicillin, and the amount may be cumulative, because destruction of the dried penicillin in dust may be relatively slow, and the penicillin would continually be redistributed through disturbances of dust and air and the handling of articles.

Appreciable amounts of penicillin were shown to gain access to the nares of persons working in the hospital environment, and without doubt this will inhibit the growth of penicillin-sensitive strains of Staphylococcus aureus. Such persons will be continually exposed to recontamination with staphylococci from the environment, the great majority of which in hospital will be penicillinase-producing strains. Penicillin-resistant strains will, therefore, find it easy to establish themselves and to colonize the nares of a larger number of persons in hospital than in environments which do not contain penicillin. The environment of the factory handling penicillin was similar to that of the hospital in that it contained penicillin and all the carrier strains of Staph. aureus were penicillin-resistant. Environmental penicillin is an important factor in the colonization of hospital nasal carriers with penicillin-resistant Staph. aureus and in the cross-infection of persons receiving or not receiving penicillin therapeutically.

Changes in the Level of Serum Glutamic Oxaloacetic Transaminase in Myocardial Infarction. P. Fortin, R. Bourdon, J. van Vonterghem and Y. Bouvrain. Bull. soc. méd. hôp. Paris 74:9-20 (No. 1 and 2) 1958 (In French) [Paris].

Measurements of serum transaminase activity were made by the authors in 9 patients hospitalized for a painful thoracic syndrome that had led to a diagnosis of myocardial infarction. Their findings were in harmony with those previously reported by others. The level of transaminase was almost always increased, and the results differed little from patient to patient. The rise in the serum glutamic oxaloacetic transaminase took place early, within the first 24 hours and usually about the 6th hour. The level reached a maximum of 2 to 10 times the normal 24 to 48 hours after onset, return-

ing to normal rapidly and constantly on the 5th or 6th day. Myocardial infarction is not the only condition in which there is an increase in the serum glutamic oxaloacetic transaminase level; in particular, care must be taken to ascertain that the patient is not in a state of hepatic insufficiency. The diagnostic significance of increased serum transaminase in myocardial infarction, however, is indisputable, especially in difficult cases, such as those involving extension of a recent infarct or those in which the presence of earlier lesions makes it hard to interpret the electrocardiographic tracings. The measurements should be made as soon as the condition is observed, and they should be repeated daily, if possible, up to the 8th day. A rise in the serum transaminase is less valuable from the prognostic point of view, because, although the amount of the increase is apparently proportional to the extent of the necrosis, the size of the infarcted area is not the only element affecting the prognosis in patients with myocardial infarction.

Action of a Preparation of Gastric Mucin in Lowering Serum Concentrations of Lipids. L. Cucurachi and A. G. Dettori. Minerva med. 48:4503-4512 (Dec. 26) 1957 (In Italian) [Turin, Italy].

Variations in serum concentration of lipids and cholesterol produced by a preparation of gastric mucin were studied in 3 groups of a total of 40 hospitalized patients of both sexes, between the ages of 36 and 72 years. The first group consisted of 12 patients with diabetes associated with atherosclerosis, the second group consisted of 18 patients who had general atherosclerosis with prevalent myocardial localization, and the third group consisted of 10 patients with various disorders, such as obesity, glomerulonephrosis, and essential hypertension. The preparation was given orally, in 3 divided doses of 100 mg. each, after meals for a period between 20 and 40 days. Determinations of total serum cholesterol, cholesterol esters, fatty acid, and, in some instances, phospholipids were made in patients in fasting state 10, 20, 30, and 40 days after beginning of the treatment. The preparation brought about gradual decrease of total serum cholesterol, cholesterol esters, and fatty acid values during the treatment, which was already noted at the first test taken 10 days after beginning of the treatment. These values tended to increase after discontinuance of the therapy. Since the preparation of gastric mucin was well tolerated by the patients, the authors suggest its use for prolonged periods of time.

The best results were noted among the patients with diabetes; all responded to the treatment in varying degrees. Patients with general atherosclerosis showed less or no response. Patients of the third group showed the least satisfactory results. Mean decrease of fatty acid values was larger than mean decrease of total serum cholesterol values in the first 2 groups. The preparation of gastric mucin has thus proved to have the effect of normalizing the serum concentrations of lipids and cholesterol.

Variants of Kartagener's Syndrome in the Same Family. E. L. Overholt and D. F. Bauman. Ann. Int. Med. 48:574-579 (March) 1958 [Lancaster, Pa.].

The authors report on a family consisting of 6 members, the 40-year-old father, the 39-year-old mother, 2 sons aged 13 and 8 years, and 2 daughters aged 14 and 5 years, 5 of whom had incomplete forms of the syndrome described by Kartagener as the triad of situs inversus, bronchiectasis, and chronic sinusitis. The father had only chronic sinusitis, and the mother had always been in good health. The 14-year-old daughter had agenesis of the frontal sinuses, underdeveloped paranasal sinuses, sinusitis, nasal polyposis, and bronchiectasis without dextrocardia; she did not have bronchiectasis when a bronchogram was made at the age of 6. The 5-year-old daughter had complete situs inversus, sinusitis, underdeveloped paranasal sinuses, chronic bronchitis, and fibrosis of the lower lobe of the left lung; she did not yet have bronchiectasis. The 2 boys had sinusitis only. It appears that bronchiectasis and sinusitis are acquired, although the familial tendency indicates a definite antenatal influence. The exact nature of the respiratory defect or the manner of inheritance is not clear on reviewing the literature. In the families described by other workers and by the authors, it is apparent that Kartagener's syndrome can occur in various combinations within the same family. The importance of early recognition and prompt therapy is reemphasized.

Serologic Diagnosis of Brucellosis: Certain Effects of Epinephrine. G. Frada, Minerva med. 48:4493-4499 (Dec. 26) 1957 (In Italian) [Turin, Italy].

Experiments have shown that epinephrine often produces an increase in value of the Wright agglutination test or elicits a positive from a previously negative agglutination test. This phenomenon has induced the author to use epinephrine during the past few years. The case of a woman, 45 years old, who had a chronic form of brucellosis is presented. The first clinical signs of the disease appeared 2 years before admission to the clinic. The disease had never been completely cured, and intermittent febrile periods occurred. This was probably due to incongruous antibiotic medication. On admission, treatment with epinephrine in daily dosage of 1/50 mg. administered intravenously for several weeks was instituted. Before the injection the agglutinin titer was 1:320; it rose to 1:1280 5 minutes after the injection during the first few days of treatment. The increase in agglutinin titer was accompanied by the paradoxical phenomenon with the

prozone ranging from 1:10 to 1:320. These readings were unaltered after heating the serum at 56 C for 30 minutes. After several days of treatment, the agglutinin titer decreased to 1:320 both before and after the injection of epinephrine, and the paradoxical phenomenon disappeared. The spleen was enlarged on admission, but its size was reduced to physiological limits at the end of the epinephrine therapy. The patient was free from all symptoms of brucellosis after termination of the therapy.

Familial Ulcerative Colitis and Ileitis. E. A. W. Houghton and J. M. Naish. Gastroenterologia 89:65-74 (No. 2) 1958 (In English) [Basel, Switzerland].

The authors report on 7 families from the Bristol area in England, in which there were 14 proved cases of ulcerative colitis and 4 cases of regional ileitis. Two members of 3 families and 3 members of 1 family had ulcerative colitis. Of 2 brothers in 1 family, 1 had ulcerative colitis and 1 regional ileitis. In 1 family of 3 generations, 4 members had ulcerative colitis and 1 had regional ileitis. In the 7th family, 2 members had regional ileitis for which an ileotransversostomy was performed, after which there was a recurrence with involvement of the colon. From an analysis of hospital admissions in the Bristol area, an estimate was made of the incidence of the 2 diseases in the general population; it showed a rate of 0.85 per 1,000 for ulcerative colitis and a rate of 0.14 per 1,000 for regional ileitis. These data strongly suggest that the reported familial incidence is not coincidental. It seems safe to assume that a hereditary predisposition exists for both diseases and that it is not possible to draw a sharp dividing line between ulcerative colitis and regional ileitis. The hereditary factor, together with the variability of the clinical picture, the occurrence of mild cases, the frequently relapsing course, the wide range of histological findings, and the suppressive effect exerted by corticoid preparations, makes an allergic basis likely in both diseases.

Jaundice, Hyperlipemia and Hemolytic Anemia: A Heretofore Unrecognized Syndrome Associated with Alcoholic Fatty Liver and Cirrhosis. L. Zieve. Ann. Int. Med. 48:471-496 (March) 1958 [Lancaster, Pa.].

Twenty men, between the ages of 26 and 65 years, with alcoholism, who were observed at the Minneapolis Veterans Administration Hospital in the course of the last 8 years, showed an interesting group of manifestations heretofore not recognized as a distinct syndrome with a predictable course. Anorexia, nausea or vomiting, diarrhea, and weight loss were common. Malaise, weakness, cough, and chilliness were also frequent. Upper abdominal pain was almost always present but varied in severity. Low-grade fever lasting several weeks after admission was the rule. Tremulousness was common, and frank delirium tremens occurred occasionally. The essential clinical features were jaundice, hyperlipemia or hypercholesterolemia, and hemolytic anemia. The illness followed excessive drinking, and improved rapidly once the drinking stopped. The hyperbilirubinemia and hypercholesterolemia receded over a few weeks. Hemolysis was generally slight and of short duration. The anemia was mild and did not persist. Hepatic function was usually mildly disturbed and improved rapidly. Liver biopsy specimens were obtained from 16 patients; fatty infiltration was evident in the livers of 14 patients, and minimal to moderate portal cirrhosis in those of 15 patients.

The patients generally presented diagnostic problems until the syndrome was defined. Obstructive jaundice was often suspected initially, and exploratory laparotomy was performed on 1 patient. The anemia was always recognized; however, hemolysis was usually not suspected. Repeated examinations of stools for occult blood were made, with negative findings. In 1 patient the hemolytic anemia was extensively studied without recognition of the related alterations in blood lipids or in hepatic function. The mechanism of the hemolytic anemia is unknown. The hemolysis seems to be related to the hyperlipemia, and an abnormal lipid may be present.

Tetanus of the Adult in the Hospital Civil of Guadalajara: Clinical Picture and Treatment. A. Ruiz Sánchez and F. Ruiz Sánchez. Arizona Med. 15:103-104 (Feb.) 1958 [Phoenix].

The authors report on 42 men and 23 women with tetanus, who were treated at the Hospital Civil of Guadalajara, Mexico, between 1952 and 1957. Most of the patients were between the ages of 10 and 50 years. Seventeen of the 65 patients died within the first 36 hours of treatment. The period of incubation varied from 1 to 4 days up to 2 or 3 months. In general, the shorter the period of incubation, the more severe the clinical picture. The clinical picture was characterized by tonic tetanic spasms of the muscles of mastication and the spinal muscles. Trismus was present in 45 (93%) of the 48 patients who survived the first 36 hours of treatment. Subintrant paroxysms were observed in 44 (92%), opisthotonos in 39 (81%), rigidity of the nape of the neck in 36 (75%), and fever in 42 (87%). Patients with a consistently high fever died.

Treatment was practiced as follows. For the first 3 to 6 days 60,000 to 100,000 units of tetanus antitoxin was given, but evaluation of its effect was not possible, since the course of the disease in the patients who did not receive tetanus antitoxin did not differ from that in the patients who were treated

with tetanus antitoxin. Chemotherapy consisted of administration of penicillin and streptomycin and was combined with supportive treatment, including relaxing agents, sedatives, cardiovascular stimulants, administration of fluids, and administration of oxygen when needed. Attention was paid to the air passages, and tracheotomy was performed when necessary. For cortical sedation, chlorpromazine hydrochloride was given in doses of 25 mg. once or twice a day by the intramuscular route. It apparently produced a better sedation than the barbiturates, which were used in 29 patients and were given in doses of 0.15 to 0.30 Gm. intramuscularly every 6 hours in the early stage of the disease and once or twice a day thereafter. The use of diphenhydramine (Benadryl) hydrochloride by either the oral or the intramuscular route in doses from 50 to 200 mg. has been considered advisable.

In the group of patients treated for more than 48 hours, the mortality was reduced to 33%. If the patients who died within the first 36 hours were included, the mortality rate was 50%. In general, mortality was higher in women patients between the ages of 20 and 30 years, in those in whom the portal of entry was through a wound produced by a sharp instrument or hypodermic needle, in those with a short incubation period, and in those with a severe clinical aspect. The predominant complications were of two types, those related to the illness itself, such as respiratory paralysis, laryngeal spasm, asphyxia, heart failure, etc., and those which occurred as a result of treatment, the anaphylactic reactions and oversedation in those patients with respiratory complications.

Vitamin B_1 Treatment of Gastric and Duodenal Ulcer. V. I. Ivanov-Neznamov. Klin. med. **36**:133-139 (Jan.) 1958 (In Russian) [Moscow].

The author treated 158 patients with gastric ulcer and 184 patients with duodenal ulcer with vitamin B_1. A control group, treated dietetically only, consisted of 30 patients with gastric ulcer and of 77 patients with duodenal ulcer. Investigation of the presence of vitamin B_1 in 150 patients with gastric ulcer showed its deficiency in 73.3%. One hundred fifty patients with duodenal ulcer showed deficient vitamin B_1 in 69.3%. Forty-two patients with either gastric or duodenal ulcer showed, together with deficient vitamin B_1 in the 24-hour specimen of urine, an increase in pyruvic acid. Clinical, roentgenologic, and gastroscopic studies of the material established the healing of the gastric ulcer in 92% and of the duodenal ulcer in 86%. Clinical and anatomic healing of the gastric and the duodenal ulcer in the control group was observed in only 40.4% of the patients.

Vitamin B_1 therapy shortened the hospital stay of the patients from the usual 45-50 days to 32-35 days. Vitamin B_1 is more effective in the treatment of ulcerative disease in doses of 25 mg. given subcutaneously 2 to 3 times daily in the course of 30 to 35 days. The diet is of the mechanical and chemical sparing type. Animal albumin in the amount of 2 Gm. per kilogram of weight helps correct vitamin B_1 hypovitaminosis. Clinical, roentgenologic, and gastroscopic observations showed that the duration of cure of ulcer disease under the influence of vitamin B_1 does not exceed the average of 32 days for ulcer of the stomach and 35 days for ulcer of the duodenum. Painful ulcer syndrome disappears, as a rule, during the first 3 to 5 days of the treatment; dyspeptic and gastric manifestations disappear during the first 6 to 8 days. Gastric acidity increases in antacid and subacid gastritis and diminishes down to normal figures in hyperacid gastritis. The gastroscopic appearance of gastritis becomes normal more often in gastric ulcer, even though the gastritis persists longer than the ulcer. Recurrences have been noted in not more than 15% of the patients. They were somewhat more frequent in those with duodenal ulcer.

SURGERY

Lingular Disease Simulating the Right Middle Lobe Syndrome: Report of a Case. D. E. Storey. J. Indiana M. A. **51**:303-309 (March) 1958 [Indianapolis].

The author reports on a 40-year-old woman with 2 attacks of pneumonitis at an interval of 6 weeks, for which she was given antibiotic therapy; this resulted in the disappearance of symptoms but not in the clearing of a lesion in the lingular segment of the upper lobe of the left lung, shown by the chest roentgenogram. Two months later the patient again had pain in the left side of the chest, a cough productive of yellow purulent material, rise in temperature to 99.4 F (37.5 C), and considerable clouding of the lingular segment on roentgenologic examination. Bronchoscopy did not show significant abnormal findings in the right and left main bronchi, but there was a moderate amount of mucopurulent exudate aspirated from the region of the lower lobe orifice. Thoracotomy was performed, and on opening the pleural cavity on the left the lingular portion of the left upper lobe was found to be atelectatic and involved in a chronic suppurative process. During dissection of this, an obstructive broncholith, measuring about 1.5 cm. in diameter, was found in the superior branch of the lingular bronchus. The lingular portion of the left upper lobe was removed. There were no other significant gross abnormal findings in the left lung. The clinical picture and roentgenologic findings were considered to be the result of chronic obstruction due to the presence of the concretion. Pathological examination of the surgical specimen revealed pneumonitis and bronchiectasis. The postoperative

course of the patient was uneventful, and for about 2 years after the operation she had no recurrences of her respiratory symptoms and no further attacks of pneumonitis.

A review of the Anglo-American literature for the past 10 years and pertinent papers before that time failed to reveal any cases of isolated lingular disease due to an obstructive broncholith. The middle-lobe syndrome and its symptom complex are well recognized, and the possibility of the diagnosis is always considered whenever disease occurs in the lower chest on the right. Isolated lingular disease with a similar symptom complex is definitely less well known and apparently seldom recognized. The causation of isolated lingular disease is probably not as variable as that of the middle-lobe syndrome, but still the condition is presumably due to either intraluminal or extraluminal causes, such as are seen in the middle-lobe syndrome. The anatomy of the middle-lobe bronchus and the anatomy of the bronchus to the lingular segment of the left lung are definitely different, and this fact explains the definitely smaller number of isolated cases of lingular disease. As in the case of the middle-lobe syndrome, the definitive diagnosis of isolated lingular disease can be made only by surgery and after examination of the resected specimen. Clinical bronchoscopy and roentgenologic findings are important in the preoperative preparation of the patient, but a definitive diagnosis cannot be made on these findings alone.

958
167

Results of Surgical Treatment for Carcinoma of the Stomach at Denk's Clinic in Vienna. H. Denk and F. Helmer. Gastroenterologia **89**:19-37 (No. 1) 1958 (In German) [Basel, Switzerland].

Of 863 men and 566 women, between the ages of 21 and over 80 years, with carcinoma of the stomach, 1,246 (87.2%) were operated on at the second surgical clinic of the University of Vienna, and 97% of them were followed up between 1933 and 1955. The results of surgical treatment obtained in these patients were critically examined. In 63.1% of the patients complaints had existed for a longer period than 3 months before admission to the clinic. Forty-six per cent of the patients disregarded the early symptoms, and in 54% the physician-in-charge failed to make an early diagnosis. Of the 1,246 patients operated on, 372 underwent an exploratory laparotomy, and 256 had palliative operations (gastroenterostomy and gastrostomy). Six hundred eighteen patients (43%) had gastric resection. The primary operative mortality rate after subtotal resection, according to Billroth 1 or 2, was 16.8%, after resection of the gastric cardia 32.5%, and after total gastrectomy 33.6%. Almost 50% of the deaths were caused by insufficiency of suture and peritonitis. Of the 618 patients with total resection, the operation was not radical in 29, i. e., it did not include resection of lymph-node metastases. Of the remaining 589 patients, 126 died and 463 were discharged; 43 of these could not be traced, which left 420 patients who were followed up. Sixty-seven and five-tenths per cent died within 1 year after the operation, 46% within 2 years, and 28% within 5 years.

As to postoperative results, patients with corpus carcinoma have the most favorable life expectancy, while those with carcinoma consisting entirely of connective tissue and with carcinoma of the cardia have the least life expectancy. The tumors with localized growth (types 1 and 2), according to Borrmann's classification, have a 50% better prognosis than the infiltrating carcinomas (types 3 and 4). The incidence of recurrence of the tumor in the anastomosis and in the stump, respectively, was 16% in the patients with type 1 and type 2 carcinoma and 84% in those with type 3 and type 4 carcinoma.

Concerning postoperative functional disturbances in the absence of recurrence, the patients were divided into 4 groups: those who were completely free of complaint (83.4%); those with mild complaints which could be relieved by diet alone (13%); those with moderate complaints despite adequate diet (1.8%); and those with severe complaints (1.8%). A dumping syndrome was observed in 31%, regurgitation in 35%, and vomiting in 4%. Dysphagia was observed in 50% of the patients who had undergone total gastrectomy and esophagojejunostomy and in 20% of those with resection of the cardia. These data suggest that reflux of the chyme, particularly in the presence of disturbance of motility, rather than regurgitation of the acid gastric juice, may be responsible for the dysphagia. The authors' findings show that from the practical point of view total gastrectomy does not provide substantial improvement in prognosis. Total gastrectomy is indicated only in patients with the infiltrating forms of carcinoma of the stomach (Borrmann's types 3 and 4) without lymph-node metastasis (relative indication) or in those in whom the size of the tumor makes it imperative (absolute indication).

Emergency Gastrectomy for Acute Gastroduodenal Perforation. E. J. Cerise. J. Louisiana M. Soc. **110**:67-71 (March) 1958 [New Orleans].

In January, 1953, a deliberate change in the policy of management of acute gastroduodenal perforation was made by the surgical service in Tulane University School of Medicine at Charity Hospital of Louisiana in New Orleans. This change consisted in the performance of immediate subtotal gastrectomy instead of simple closure in all suitable cases. Only the good-risk patients were submitted to gastrectomy, whereas, the more critically ill were treated by simple closure. From January, 1953,

through May, 1957, there were 96 patients on the Tulane surgical service treated by surgical measures. Of these, 46 had simple closure of their perforation, with 6 deaths, a mortality rate of 13%. The remaining 50 patients had subtotal gastrectomies, with 1 death or a 2% mortality rate. This 1 death resulted from a transfusion reaction. The 50 gastrectomies were regarded as technically easy, as the associated edema often facilitated the dissection. However, in 2 instances, due to the reaction and scarring in the area, tube duodenostomy was necessary. The standard Billroth 2 technique was usually followed.

One of the 46 patients treated by simple closure began to bleed shortly after operation and required emergency gastrectomy on the 6th postoperative day for control of hemorrhage. This case deserves special mention, because it emphasized the possibility of simultaneous acute peptic ulcers on the anterior and the posterior wall of the duodenum. In the 50 gastrectomies, an additional posterior ulcer was noted in 7 cases. This incidence of at least 14% multiple ulcers is recently becoming appreciated in perforations with hemorrhage. The author lists the following as absolute indications for gastrectomy in acute perforations: (1) carcinoma of the stomach (delimited resectable lesions); (2) associated with recent or simultaneous gross hemorrhage; and (3) associated with fixed pyloric obstruction. In addition, from the knowledge gained by follow-up studies, the author regards the following as justifiable indications: (*a*) recurrent perforations and (*b*) a definite previous ulcer history (more than 6 months) and in the younger age groups (under 50 years). The author concludes that a more aggressive attitude than simple closure is necessary, but the routine use of gastric resection seems unwarranted. It is suggested that certain criteria based on the condition of the patient and his prognosis be used to determine the appropriate treatment.

Treatment of Endarteritis Obliterans by Intra-Arterial Blood Infusion. N. V. Rozovsky. Khirurgiya 33:53-59 (No. 12) 1957 (In Russian) [Moscow].

This method of treating endarteritis obliterans consisted of infusing from 200 to 250 cc. of blood into the femoral artery of the patient under a pressure of 40 to 60 mm. Hg higher than the patient's blood pressure. The infusion was performed 2 to 4 times, with an interval of 5 to 6 days. The treatment given to 101 patients gave considerable improvement in 66%, some improvement in 25%, and no improvement in 9%. Good results were obtained principally in young patients. Adults with pronounced arteriosclerosis were not benefited by this treatment. In the younger patients the extremities after intra-arterial blood infusion became warm and of normal color. There was considerable improvement in the circulation in the extremities and in the myocardium and also in the electrolyte content and the viscosity and coagulation time of the blood. A follow-up ranging from 6 months to 6 years in 71 patients revealed recovery or pronounced improvement in 25%, improvement in 12.3%, relapse in 11.6%, amputations in 4.4%, and lethal outcome in 6.5%. A number of patients will require repeated blood infusions after a lapse of time.

Acute Forms of Regional Enteritis (Diagnosis and Treatment). M. P. Détrie. J. chir. 75:156-174 (Feb.) 1958 (In French) [Paris].

Acute terminal ileitis may appear in any of the 3 well-known clinical forms and in a less common but severe form called the necrotizing form. The pseudoappendicular form is benign and corresponds to a simple edematous lesion; the symptoms suggest acute appendicitis, but the condition may be differentiated by the occurrence of diarrhea, which is rare in ordinary adult appendicitis but is characteristic of terminal ileitis. This form of the disease frequently undergoes resolution, but in patients over 30 years of age it may be the prelude to a prolonged chronic condition. The peritoneal form, producing the picture of peritonitis due to perforation, which may or may not be present at operation, is rarer and much more severe, as shown by the occurrence of 4 deaths in 1 series of 10 cases. The occlusive form with acute obstruction of the terminal small intestine is rare. Its onset is characterized by violent pains progressing to paroxysmal attacks. Diagnosis is facilitated by the inflammatory course of the occlusion, which progresses with fever and a certain amount of abdominal contraction. Other forms of acute regional enteritis are those affecting the jejunum, the cecum, the duodenum, and the colon, either separately or in various combinations. The postappendicular form is one in which a clinical pseudoappendicular syndrome was not recognized at the time of appendectomy. Surgical treatment does not always provide protection against renewed acute attacks of the disease; recurrences, in fact, are characteristic of regional enteritis.

The diagnosis of regional enteritis is not easy. Whatever the clinical aspects, 3 factors will prove helpful in making the diagnosis: the youth of the patient, diarrhea, and an earlier appendectomy. Roentgenography may result in visualization of pneumoperitoneum in cases of perforation and may reveal the presence of fluid in patients with occlusion. Conditions requiring differentiation are acute appendicitis, typhoid, intestinal infarct, simple ulceration of the small intestine, secondary ileitis, intestinal tuberculosis, and Hodgkin's disease. Medical treatment is often disappointing, but antibiotics may be useful in complications such as peritonitis,

abscesses, and fistulas, although they have no effect on the disease itself. Administration of cortisone or corticotropin (ACTH) sometimes produces a transient cure, but this has little value in a disease characterized by recurrent attacks. Perforation and hemorrhage are sometimes caused by these hormones. Surgical treatment ranges from simple exploratory laparotomy to resections of various kinds according to the site of the lesion. Surgical treatment is not indicated when the diagnosis of the appendicular form is made before operation, but if the diagnosis is made during laparotomy, the operation should be limited to a simple survey of the lesions, and no resection or short-circuit procedure should be attempted. Resection in spite of a fairly high mortality is possibly the best procedure in cases of perforating or necrotizing enteritis. The occlusive forms require emergency treatment, such as resection, simple freeing of the loop, or internal or external derivation, depending on the general condition of the patient and the change in the intestinal segment. Various special operations, such as gastrojejunostomy, may also be used with good effect in certain localizations.

Surgical Treatment by Spongiosa Plombage of Juvenile Patients with Bone Cysts. H. Hellner. Chirurg **29**:97-103 (March) 1958 (In German) [Berlin].

The author reports on 5 patients, between the ages of 6 and 15 years, with bone cysts occurring in the upper metaphysis of the humerus and of the femur or in the diaphysis of the humerus, who were operated on by filling the cavity in the bone with spongy substance obtained from the ventral surface of the patient's ilium. The fluid was removed from the cavity and the spongy substance introduced into it through a small opening made in the wall of the cyst with the aid of a chisel; this opening makes stripping of the connective tissue membrane possible. Excellent results were obtained. Deficient fixation, functional impairment, infection, or refracture requiring a secondary operation was not observed in any of these 5 or all the other juvenile patients with bone cysts of the humerus, femur, or tibia who in the last 6 years were operated on according to this technique. The method was also used successfully for the treatment of patients whose bone cavities did not contain fluid but fibrous giant-cell (osteoclast) tissue with small active foci of decomposition of bone. In only 1 patient the additional use of a pin was required for stabilization.

The results of plombage with spongy substance are superior to those of purely conservative treatment with an abductor plaster-of-paris dressing which is unreliable. Plombage with spongy substance is preferred to treatment by apposition of thick pieces of cortical substance or ribs. Nailing alone is not recommended. True recurrences, i. e., definite progressive decomposition of bone or a zone of transformation associated with the risk of spontaneous fracture, were not observed after plombage with spongy substance. The latter is the method of choice for the treatment of bone cysts with or without areas of giant-cell–fibrocyte tissue.

Implantation Recurrence of Carcinoma of Rectum and Colon. L. P. Le Quesne and A. D. Thomson. New England J. Med. **258**:578-582 (March 20) 1958 [Boston].

Cancer cells implanted onto a raw tissue surface are capable not only of surviving there but also of growing and forming a metastatic nodule. Such recurrences have been described after operations for carcinoma of the breast, bladder, and ovary. In addition, it is now apparent that in lesions of certain hollow viscera similar implantation recurrences may occur, even though the operation has in no way transgressed the limits of the growth, as the result of the shedding of viable tumor cells into the lumen of the viscus. In particular, this complication is apt to occur after operations for carcinoma of the large intestine. The danger of this type of recurrence is exemplified by the 3 cases presented in this paper. In the first of these 3 patients a recurrence at the suture line was due to implantation of malignant cells during the original operation. In the second patient the carcinoma was at the site of the upper end of the lateral hemorrhoidectomy wound on the left. Although it was possibly a second primary growth, it was regarded as resulting from implantation of malignant cells onto the raw hemorrhoidectomy wound. This supposition was supported by the entirely superficial situation of the tumor. The third patient had a recurrence in the perineum after an abdominoperineal excision. Despite the early invasion of the perirectal fat, the initial excision appeared complete, and it seems most likely that the recurrence should be ascribed to implantation of malignant cells spilt into the wound as a result of accidental opening of the rectum close to the growth during the first operation.

Recurrence of the growth at the intestinal suture line is now a well-established hazard after operations for carcinoma of the large intestine that involve excision of a portion of the colon followed by restoration of intestinal continuity by an immediate anastomosis. It is clear also that recurrences at the suture line after restorative operations are due not to inadequate excision of the primary tumor but to implantation onto the cut edge of the intestine of viable tumor cells shed into the lumen. This desquamation of malignant cells takes place not only during handling of the growth at operation but also

during the weeks and months that the tumor is present before diagnosis and treatment. Evidence of this continual shedding of viable cells is provided by the many well-authenticated cases of implantation of carcinoma of the intestine in the track of a preexisting fistula in ano. The prevention of implantation of carcinoma is discussed not only with regard to restorative operations but also with regard to the importance of not performing any operation on the distal part of the intestine until the primary tumor has been removed. The latter point is of greatest significance in relation to benign adenomas found on sigmoidoscopy distal to a carcinoma. It is wise to delay their removal until after excision of the proximal part of the malignant tumor.

Patellectomy: Repair by Quadriceps Tenoplasty. H. O. Marsh, H. O. Anderson and O. Pliego. Am. Surgeon **24**:273-279 (March) 1958 [Baltimore].

Marsh and associates employ the standard anteromedial incision for their technique of patellectomy with quadriceps tenoplasty. The patella is excised by sharp dissection, preserving all healthy soft tissue, and all debris is removed from within the joint. The surgical defect is repaired with the knee in extension, plicating the capsule transversely under slight tension with mattress sutures. A triangular tongue of tendon from the superficial layer of the quadriceps tendon (that of the rectus femoris) is reflected distally. The apex of this tendon flap is 4 in. above the former patellar site, and the base is 2 in. in width. The reflected portion of the quadriceps tendon is split longitudinally into 2 equal segments in a sagittal plane. A small hemostat is forced transversely through the mid-point of the patellar tendon creating a tunnel. The reflected tendon strips are drawn through this opening from the respective medial or lateral side and sutured under moderate tension. Superficial to the patellar tendon, the tails of the tendon flaps are again crossed and sutured. The edges of the tendon donor site are approximated with interrupted sutures. After wound closure, a pressure dressing is applied to minimize postoperative swelling, but the knee is not immobilized. Quadriceps muscle exercises and active knee motion are initiated on the first postoperative day. The patient is encouraged to be as active as possible. Crutch walking is started on the 4th or 5th day and continued for 2 or 3 weeks, after which the patient is ambulatory without support.

During the past 15 years the authors employed this method of patellectomy on 36 knees in 31 patients. There were 14 knees with acute patellar fractures (including simple, complicated, and compound fractures), 9 cases of osteoarthritis, 5 patients with severe chondromalacia, 2 with nonunion or malunion, and 6 with recurrent dislocation of the patellar with degenerative joint disease. The authors were able to examine 27 knees at follow-up examinations, and information on the condition of 5 other knees was obtained by letter; the remaining 4 knees were lost to follow-up. The power in the patellectomized knee was always less than that in the knee not operated on. This decrease in strength was secondary to the loss of the patellar pulley action. Quadriceps atrophy was demonstrable in all cases. Diminution of quadriceps power and some atrophy was undoubtedly present in a number of patients preoperatively. The rapidity with which quadriceps power and good knee function was regained was directly proportional to the patient's diligence in his rehabilitation program. There was a complete range of active knee motion in 11 patients, while in the remaining 25 there was some loss. Limitation of knee motion had been anticipated preoperatively in many of these patients. The authors believe that knowledge that a patellectomy will not restore a knee to normalcy in certain disabling conditions should not deter the surgeon from its employment given the proper indications. A knee incapacitated 50% by osteoarthritis, chondromalacia, or traumatic incongruities of joint surface and restored to a 15% disability is a highly successful result. The authors list the following indications for patellectomy: (1) comminuted fractures; (2) malunited fractures; (3) nonunion; (4) advanced osteoarthritis of the patellofemoral mechanism; (5) chronic symptomatic chondromalacia; and (6) recurrent dislocation with degenerative changes.

Colloid Carcinoma of the Colon in Children. J. A. Buchman and J. D. Calhoun. Am. Surgeon **24**:280-286 (March) 1958 [Baltimore].

The authors were able to collect 50 cases of proved carcinoma of the large intestine (excluding rectum and rectosigmoid) in patients 16 years of age or under. They believe that the true incidence is probably higher than this number suggests. Two illustrating case histories are described. The first was that of a 15-year-old boy in whom the roentgenologist reported a complete obstruction of the colon in the upper sigmoid area which corresponded to a palpable mass. At operation the boy was found to have a large mucoid type of carcinoma of the upper sigmoid colon with a small liver metastasis. A radical resection was done. The patient survived 6 months and died of diffuse carcinomatosis.

The second case history presented was that of a 13-year-old girl who had had vague epigastric and paraumbilical pain for 3 months. Pain was severe for 10 days, and there was nausea and vomiting for 8 days. The abdomen was opened through a McBurney incision, the incision was extended,

and the diagnosis of carcinoma of the colon was established. The colon was decompressed. Ten days later a radical resection was done for a mucoid carcinoma of the splenic flexure. Twenty-six months later rectal examination revealed a movable mass in the cul-de-sac. A large Krukenberg tumor of the left ovary was removed. The patient had gross metastases to other abdominal organs, and she died 4 months later of generalized carcinomatosis.

The incidence of carcinoma of the colon was most frequent in 12-year-old children. One child was only 3 years old. Boys greatly predominated over girls (35 and 15 cases respectively). The distribution of the primary site of growth in the children studied was essentially the same as in adults. There is no explanation for the increased frequency of carcinoma in the pelvic colon, which is found both in children and in adults. In general, malignant diseases in the young are more virulent than in adults. This is also true of carcinoma of the colon. The fact that, in 20 of the 46 children in whom the lesion was examined microscopically, the diagnosis was colloid or gelatinous carcinoma indicates that the incidence of colloid carcinoma of the colon is much higher in children than in adults (46% compared with 5% or less). The treatment of carcinoma of the colon in children is the same as in adults, except that the operative procedure should be more radical in children than in adults. Most of the children reported had been treated for many months before the exact diagnosis was established. It is hoped that the unfavorable prognosis can be improved with earlier diagnosis.

Results of Surgical Treatment of Patients with Phantom Limb Pain. R. Wüllenweber. Chirurg **29**:115-118 (March) 1958 (In German) [Berlin].

According to the author, surgical methods employed at the neurosurgical clinic of the University of Bonn for the treatment of phantom limb pain were based on an interruption of the pain paths between the periphery and the pain centers in the thalamus and the cerebral cortex respectively. Obliteration of the peripheral nerves by injections of alcohol was performed on 33 patients. It is the most sparing method which places the smallest load on the entire organism. Eighteen of the 33 patients obtained temporary improvement, but repeated surgical intervention became necessary later. Of 12 patients who were followed for several years, considerable improvement continued postoperatively for 2 years in 6, but only 2 were completely free of pain for more than 5 years. In 1 patient whose forearm was amputated, the phantom limb pain subsided, but the stump remained painful. Foerster's operation of cutting intradurally the thoracic nerve roots, a major operation associated with risk of injury to the spinal cord and loss of spinal fluid, was performed on 10 patients, 9 of whom had undergone various previous operations on the peripheral nerves. Follow-up examinations were performed 3 to 10 years after the Foerster operation in 9 patients, and not a single patient was completely free of pain. Postoperative improvement lasted for several weeks or months only. Sympathectomy was performed on 15 patients between 1946 and 1950; 8 of these patients were subjected to cervicothoracic sympathectomy, and 7 underwent lumbar sympathectomy. All these patients showed clinical signs of changes in the autonomic nervous system. Sympathectomy had no effect on the phantom limb pain in 3 patients. Of 13 patients who were reexamined 1 year after the operation, only 2 were free of pain. Of 12 patients who were followed for 7 to 12 years, only 1 was completely free of pain.

Unilateral (contralateral) or bilateral spinothalamic chordotomy was performed on 10 patients. Two patients were therapeutic failures, but 8 were improved by the operation and remained free of pain for 1 to 3 years after the operation. Only 1 patient remained free of pain for more than 7 years, and up to now there has been no recurrence of pain; this patient was able to resume his work as an industrial worker. Psychotherapy preceded chordotomy in 2 patients but was ineffective. Psychotherapy after chordotomy was practiced in 1 patient but resulted in only minor improvement. The reported data show that the late results of surgical treatment of phantom limb pain are poor. Consequently, more conservative methods, such as procaine hydrochloride infiltration of the peripheral cerebrospinal and sympathetic nervous system, and "pharmacological leukotomy" with phenothiazine derivatives, such as promethazine (Atosil), were performed on a larger scale with satisfactory results; however, long-continued improvement was not observed. Intensive psychotherapeutic treatment seems to be justified.

Aortography in Diagnosis of Diseases of the Thoracic Aorta. G. A. Natsvliskvili. Khirurgiya **34**:92-97 (No. 1) 1958 (In Russian) [Moscow].

Aortography is a valuable method of examination in diagnosis of patency of the ductus arteriosus, anomalies, and aneurysms of the aorta. Aortography aids the surgeon in solution of problems of diagnosis and surgical tactics. The author usually practices the transcarotid approach on the left. A special catheter is introduced through an opening in the common carotid artery until the arch of the aorta. The dose of the contrast medium equals 1 ml. per kilogram of body weight. Aortography was performed on 20 patients, involving 14 with suspected patency of the ductus arteriosus, 4 with coarctation of the aorta, and 2 with aneurysms of the thoracic aorta. There were no complications after this examination.

NEUROLOGY & PSYCHIATRY

Medical Treatment in Epilepsy. H. H. Merritt. Brit. M. J. 1:666-669 (March 22) 1958 [London].

The treatment of patients with convulsive seizures is divided into 3 parts: (1) removal of any factors, organic or psychological, that may play a part in the occurrence of seizures; (2) regulation of the physical and mental hygiene; and (3) administration of anticonvulsant drugs. The objective of all anticonvulsant therapy is to establish and maintain a reservoir of drug sufficient to control the seizures without producing significant side-reactions. Since the ideal anticonvulsant is not yet available, a choice must be made from a group of drugs, one or more of which is most effective for a particular seizure type or for a particular patient. When more than 1 type of seizure is present, a combination of drugs is usually more effective than a single drug. A combination of drugs will often be necessary even for patients with a single seizure type. The majority of anticonvulsants in common usage today are derivatives of barbituric acid, hydantoin, or oxazolidinedione. Other anticonvulsants commonly used at the present time include primidone (Mysoline), which has a structure similar to that of phenobarbital, succinimide derivatives, and carbonic anhydrase inhibitors. The use of these different drugs in the therapy of all types of seizures, except petit mal, are discussed.

For the successful treatment of petit mal, it is important to distinguish this seizure from other minor seizure types. The drugs commonly used for the treatment of petit mal seizures are derivatives of oxazolidine and succinimide. These drugs are not effective against other types of seizures and are thought by some to precipitate major seizure phenomena. When petit mal coexists with other seizure types, adequate therapeutic doses of phenobarbital and phenytoin sodium are indicated as well. Failure to obtain optimal results with anticonvulsant drugs is related to failure to recognize a progressive neurological disease, particularly brain tumors, failure to use proper drugs, failure to administer proper dosage, premature withdrawal of drugs, frequent shifting of drugs, poor indoctrination of the patient in regard to the therapy, and lack of recognition of the social and economic needs of the patient. The larger number of failures are related to failure to administer the proper amount of the drug and failure to use 2 or more drugs in combination. The results of treatment in 319 cases of epilepsy were as follows: controlled, 154 (48%); improved, 118 (37%); and uncontrolled, 47 (15%). The question arises as to when it is advisable to withdraw medication. The author makes it a rule to administer anticonvulsants to patients with any type of seizure except petit mal for a period of at least 3 years after all seizures have disappeared. At this time the dose of the drug can be reduced every 4 to 6 months by one-third to one-fifth of the amount required to control the seizures. If seizures recur, the drug should be readministered in full dosage. The results obtained in the attempt to discontinue anticonvulsant therapy in patients who had been seizure-free for a prolonged period have been disappointing, except for those with petit mal attacks.

Epilepsy as a Social Problem. Lord Cohen of Birkenhead. Brit. M. J. 1:672-675 (March 22) 1958 [London].

The label "epilepsy" embraces a wide range of disability and covers fits varying widely in frequency, severity, and type. At one end of the scale there is the epileptic with a history of infrequent attacks in the past, now free from attacks or with an occasional fit at long intervals; at the other end of the scale there is the epileptic with crippling motor disabilities, including paralysis and involuntary movements, and/or severe mental changes—dementia, depression, hallucinations, confusion, and severe behavior disorders. The most pressing task is educational. The public has long believed that epilepsy is synonymous with mental deficiency and uncontrollable criminal impulses, and the epileptic is thus too often treated as a pariah. These beliefs must be dispelled. The community must learn that 80% of epileptics (including those whose epilepsy follows a brain operation or injury) can, with appropriate care and encouragement, lead a normal life. Not every fit in childhood means lifelong epilepsy; 75% of children who have had fits lose them in adult life. Experience shows that under the right conditions 80% of epileptic children can be educated in ordinary schools; about 20% need special educational facilities because of mental backwardness, behavior problems, motor disabilities, frequency of fits, incontinence of urine and feces, and postepileptic automatism. If there is doubt about the suitability of the epileptic child for an ordinary school education, a "trial" term might be given. Most special schools for epileptics are residential. This is an advantage because it provides the opportunity for continuous medical supervision.

On leaving school the epileptic should be assessed with respect to his suitability for a particular job and to jobs suitable for his particular ability and gifts. Sometimes all that is needed is advice about the hazards of occupations which must be avoided. In most cases, however, resettlement in the community demands the combined knowledge, ex-

perience, and efforts of the family physician and specialists, local welfare and health officers, employment officers, and others. The unemployed epileptic tends to become depressed, morose, apathetic, and sometimes aggressive. Work, especially if it brings economic security, provides not only an interest but instills a sense of independence and responsibility which facilitates social adjustment. Some epileptics may be given vocational training at an industrial rehabilitation unit. There remains a small residue of epileptics who cannot be placed in the open labor market. For these the alternatives are employment in a sheltered workshop, home employment, or admission to a colony.

Marriage and its physical accompaniments do not aggravate epilepsy; it is often followed by improvement. Available figures suggest that, if 1 parent is epileptic, the risk of having an epileptic child is 1 in 40. This incidence may be misleading when one attempts a prognosis in the individual case. Driving an automobile may be necessary to certain types of employment, but traffic regulations preclude anyone suffering from epilepsy from claiming a driving test. But what of the epileptic whose fits have been arrested for some time? Some physicians permit the patient to drive his own car (he must never be employed as a driver on public transport) after 3 years' freedom on treatment or 2 years without any drug therapy. This is a caluclated risk, not only for the patient but also for others. However, there are exceptions, and each case should be individually assessed.

958
167

The Results of Treatment in 1,086 General Paralytics, the Majority of Whom Were Followed for More than Five Years. R. D. Hahn, B. Webster, G. Weickhardt and others. J. Chron. Dis. 7:209-227 (March) 1958 [St. Louis].

The study presented is an evaluation of the efficacy of penicillin in 1,086 patients with dementia paralytica, who were treated in a group of clinics, including Bellevue, Boston Psychopathic, St. Elizabeth's, Grady Memorial (Emory University), Johns Hopkins, New York, University of Michigan, and University of Pennsylvania hospitals. To insure uniform coding of records at the various institutions, work sheets were drawn up, and the results were transferred to punched cards. The fixed point of reference was the "study treatment" date, that treatment episode which placed the patient in the study group whether previous treatment had been given elsewhere. Patients were observed at 3, 6, and 12 months after study treatment and yearly thereafter. Of the 1,086 patients, 629 were treated with penicillin alone, and 457 with penicillin plus fever therapy, usually induced tertian malaria. The usual incubation period of dementia paralytica was 10 to 24 years after syphilitic infection. The simple dementing type of psychosis was more frequent than all other types combined. In the absence of previous treatment, the spinal fluid complement fixation reaction was always positive, and the spinal fluid cell count was almost always elevated.

None of the 1,086 patients had received penicillin for early syphilis. Paresis was not observed after penicillin treatment of asymptomatic neurosyphilis. Additive effects of fever therapy were not sufficient to justify its use. Early diagnosis and prompt penicillin treatment of incipient parasis resulted in clinical remission and ability to work in more than 80% of the patients; this treatment will prevent practically all deaths from neurosyphilis, and even the institutionalized patient has 1 chance out of 3 of improvement and rehabilitation. In contrast to the dire prognosis of untreated paresis (death within 4 years), only 9% of penicillin-treated paretics were dead of paresis 10 years after treatment. Even so, the penicillin-treated paretic patient had nearly 4 times the death rate of his or her nonsyphilitic age, race, or sex counterpart. While some symptoms of paresis were favorably influenced, abnormalities of speech, insight, calculation, judgment, and general information did not entirely disappear. Repository penicillin was as suitable as aqueous penicillin. Although the minimal effective dose is unknown, this study suggested that 6 million units is probably ample.

In general, more than 1 course of penicillin was of no demonstrable additional value. The Herxheimer reactions, notably exacerbation of the paretic pychosis or convulsive seizures, occurred more frequently in the presence of spinal fluid pleocytosis than in its absence. The Herxheimer reaction did not cause long-term damage. Posttreatment psychiatric hospitalization was directly proportional, and clinical improvement and rehabilitation for work were inversely proportional, to the severity of pretreatment psychosis. The presence at the time of treatment of incontinence, of inability to perform simple acts of personal toilet, and of convulsions afforded a particularly poor prognosis for longevity. Work status was of great prognostic import, and so was the time that had elapsed since the patient had been able to work at his usual occupation. Pretreatment pleocytosis indicated an active process amenable to treatment, but in some patients it left behind sufficient brain damage to nullify any clinical effect. The absence of pleocytosis indicated a relatively static process less susceptible of improvement. Clinical progression occurred more frequently with persistent cerebrospinal fluid cell counts of 5 to 10 per cubic millimeter than with cell counts of 4 or less. Considering that with the decreasing incidence of syphilis dementia paralytica is becoming a neuropsychiatric rarity, the authors note that these data are perhaps of more historical interest than practical importance.

PEDIATRICS

Exchange Transfusions: Experiences at University of Kansas Medical Center Over a Two-Year Period. D. S. Overend. J. Kansas M. Soc. 59:83-89 (March) 1958 [Topeka].

The author reports on 46 exchange transfusions performed on 43 infants. The conditions for which transfusion was required included hemolytic disease of the newborn due to fetomaternal incompatibility of the Rh factor or of the ABO blood groups and, in some cases, hyperbilirubinemia without demonstrable incompatibility, hereafter referred to as idiopathic hyperbilirubinemia. Rh incompatibility was demonstrable in 19 patients (44%), ABO incompatibility in 12 patients (28%), and idiopathic hyperbilirubinemia in 12 patients (28%). The incidence of prematurity was greater in idiopathic hyperbilirubinemia than in the other types of hyperbilirubinemia; 4 of 12 infants with idiopathic hyperbilirubinemia weighed less than 2,500 Gm. (5½ lb.) at birth. In the Rh group, 2 of the 19 infants were premature, while in the ABO group, only 1 of the 12 was premature.

Infants receiving exchange transfusion during the first 24 hours of life can usually be cannulated through the umbilical vein; those receiving exchange transfusions later, after the umbilical cord is no longer usable, are cannulated through the greater saphenous or the common femoral vein. Blood is withdrawn and administered in 20-ml. increments, except in the case of very ill or premature infants, when 10-ml. increments are used. At the completion of each 100 ml., 1.0 to 1.5 ml. of 10% calcium gluconate is administered through the cannula. In very small infants, 1.5 ml. of calcium gluconate is given after each 50 ml. of exchange. The calcium gluconate should be given cautiously, and the apical pulse should be constantly checked while it is given. Marked bradycardia is an indication for slowing or discontinuing the administration of calcium gluconate. Throughout the transfusion the infant is carefully observed for cyanosis, for excessive irritability which may indicate impending tetany, and for vomiting. Oxygen is administered by face mask throughout the procedure. The infant is returned to the nursery immediately after the exchange transfusion and is kept in a heated crib for 2 to 4 hours. Feeding is withheld for 4 to 8 hours depending on the condition of the infant. Antibiotics are given routinely for 48 hours after the transfusions.

Four patients in the series expired; 3 of these were referred late from other hospitals when evidence of brain damage was already present. The 4th fatality occurred at 52 hours of age after exchange transfusion at 6 hours of age; death was the result of hyaline membrane disease complicated by marked emphysema and pneumothorax. No permanent sequelae occurred in infants given exchange transfusions before the concentration of indirect bilirubin in the serum reached 15.0 mg. per 100 ml. Cannulation of the femoral or saphenous veins is often followed by cyanosis and edema of the limb, but in no case did cyanosis and edema persist for more than 48 hours. No permanent undesirable sequelae were observed in any patient after cannulation of the femoral or saphenous veins.

The presence of hydrops fetalis is an indication for immediate emergency exchange transfusion; otherwise, the decision is based on hyperbilirubinemia according to the following rules: (1) a serum indirect bilirubin level rising at a rate exceeding 0.5 mg. per 100 ml. per hour in the first 24 hours of life or exceeding 10 mg. per 100 ml. in the first 24 hours; (2) a rising indirect bilirubin approaching 20 mg. per 100 ml. at any time in the neonatal period; a lower minimum value (16-18 mg. per 100 ml.) is employed in premature infants; (3) inability of the laboratory to demonstrate blood group incompatibility does not alter the decision to perform an exchange transfusion if the indirect bilirubin reaches levels meeting either of the above criteria. Bilirubin determinations may have to be made as often as every 6 hours until the rate of rise of bilirubin concentration is established or as infrequently as every 24 hours in some patients, especially those with idiopathic hyperbilirubinemia. Studies of infants with hyperbilirubinemia have been greatly simplified by the adoption of "microbilirubin" determinations, in which the bilirubin concentration is estimated in specimens obtained by heel puncture.

The Superficial Inguinal Pouch and the Undescended Testis. P. Jones. M. J. Australia. 1:239-242 (Feb. 22) 1958 [Sidney].

The superficial inguinal pouch is an areolar space lying beneath Scarpa's fascia and in front of the external oblique aponeurosis. It is oval in outline and directed obliquely upward and laterally from the pubic tubercle. This pouch has been called the "abdominal scrotum" and varies in size. The wide range of mobility of the testis in childhood is well known, and the brisk cremasteric reflex will often retract the testis out of the scrotum. When its withdrawal is traced by palpation, it is found to have entered an extensive space situated within the fascia of the anterior abdominal wall—the superficial inguinal pouch. Such a testis is described as a "retractile testis," and while this is a convenient clinical term for a variety of normal testes, it is scarcely justifiable, as all testes in prepubertal boys are of this type. As the testis becomes larger and heavier during puberty and the cremasteric reflex becomes less brisk, the testis comes to reside permanently in the scrotum. The size of the testis prevents its passage into the superficial inguinal pouch. This constitutes the usual adult anatomy, but oc-

casionally a fascial ring larger than the testis persists, with the same clinical findings as in childhood.

The retractile testis has probably accounted for many of the successes claimed for hormone therapy in "undescended testis." Equally important is the possibility of misinterpretation of the clinical findings when a normal testis is palpable in the superficial inguinal pouch. Finger-tip manipulation will bring the testis into the scrotum, and, if this maneuver is omitted, the testis may be misdiagnosed as "undescended." There are 2 main categories of undescended testes—those arrested in the line of normal descent and those that have diverged from it. The latter are known as "ectopic testes," and 4 types are described: superficial inguinal, perineal, femoral, and penile. The superficial inguinal ectopic testis is the commonest variety, and the anatomic basis of this type is an abnormality in the attachment of Scarpa's fascia. The clinical characteristics of a superficial inguinal ectopic testis are as follows: The testis is of normal size, widely mobile within the pouch, and when it is manipulated toward the scrotum it reaches the level of the pubic tubercle and is then directed forward by the concave upper surface of the obstruction. Such a testis can never spontaneously descend into the scrotum. After commenting on uncommon variants of this type of ectopic testis, the author discusses the differentiation of a normal retractile testis from a superficial inguinal ectopic testis by the fact that there is a free communication between the pouch and the scrotum in the former which is absent in the latter. A knowledge of the normal and the abnormal anatomy is essential for accurate clinical diagnosis.

Congenital Toxoplasmosis. R. D. Montgomery, B. Donnison and H. Jolly. J. Clin. Path. 11:114-118 (March) 1958 [London].

Hydrocephalus, choroidoretinitis, convulsions, and intracerebral calcification are the 4 characteristic manifestations of congenital toxoplasmosis, but it is probable that the disease may still pass unrecognized as a cause of obscure oculocerebral defect or perinatal death. Two cases are reported. The first infant died 22 days after birth, and autopsy revealed intracellular and free forms of Toxoplasma organisms in the brain tissue. This case illustrates the remarkable pathological changes that may be found in the acute infection. The second child was spastic and microcephalic from birth. He refused to suck and developed severe ulcerative stomatitis on the third day, associated with a discharge from both eyes. When 4 weeks old, he had a series of convulsions, which persisted for a week, and thereafter remained spastic, with frequent jerks and occasional convulsions. On admission to hospital at the age of 9 months, he was found to be a microcephalic idiot, with marked microphthalmos, a small snuffy nose, and large ears. All the limbs were spastic, with flexion of the arms and hands, extension of the legs, and frequent jerking movements of the whole body. Death occurred 4 days after admission.

There is no positive evidence that the second child's condition was due to toxoplasmosis, although, if this were the case, it would represent an early burnt-out infection in which, with negative serology, one would not expect to find surviving organisms. The mother showed evidence of recent infection with Toxoplasma organisms. The mode and significance of maternal infection are discussed. Although it appears that the possible paths of infection are multiple, there is some evidence in favor of the oropharyngeal route. The only manifestation likely to give rise to the diagnosis in pregnancy is the glandular syndrome. Transplacental transmission has only been shown to occur as a result of infection acquired during pregnancy, and even in this event the degree of hazard to the fetus cannot at present be assessed. The importance of toxoplasmosis in relation to mental deficiency, microcephaly, and ocular defects may be greater than is revealed by current diagnostic criteria. The absence of serum antibodies after the first few months of life does not exclude a past infection in utero.

OTOLARYNGOLOGY

Possibilities and Results of Tympanoplasty on the Basis of 400 Operations. R. Maspétiol. Semaine hôp. Paris 34:595-598 (Feb. 26) 1958 (In French) [Paris].

Tympanoplasty is used in chronic otitis and its sequels, (1) as a reparative operation for the reconstruction of the tympanum with a skin graft and (2) as a functional procedure designed to restore the best possible auditory capacity to the ear. The successful creation of a new mobile tympanum is essential to, but not always sufficient for, the restoration of hearing. It is useless, for instance, to expect functional improvement in patients in whom a decided loss in osseous conduction bears witness to involvement of the labyrinth. Tympanoplasty in such cases can only be used as a reparative procedure, chiefly for the purpose of suppressing discharges of tubal origin. The auditory gain to be expected from the operation will depend on the preoperative audiometric curve and the extent of the anatomic lesions. An intact ossicular chain provides hope for either excellent or subnormal hearing if bone conduction is preserved, but when the ossicular chain has been destroyed, a threshold of 25 to 30 db. is the most that can be expected. Patients with a preoperative threshold of 30 db. cannot expect any elevation of this threshold after closure of the perforation in the tympanum. The

audiometric curves are sometimes abnormally good in relation to the anatomic lesions because of adhesions between an isolated stirrup, for example, and either the handle of the hammer or the vertical branch of a partially destroyed anvil. Adhesions of this kind, which play a part in the transmission of sound and which are physiologically effective, should be carefully preserved, because their inadvertent severance may have an adverse effect on the hearing. Medical treatment designed to suppress infection and to improve the general condition should always be given before tympanoplasty is undertaken in patients of any age with quiescent chronic otitis or otorrhea of tubal origin, or in children.

The present possibilities of tympanoplasty are shown by the results obtained in 100 patients with a postoperative follow-up of at least 3 months. The first 300 such operations in the author's series are not considered, because increasing experience has enabled him to obtain better results in the later cases. The indications for operation were cicatricial otitis in 48 cases and suppurative otitis in the other 52. A new mobile tympanum, with a freely aerated eardrum behind it, was obtained in 45 of the 48 patients with cicatricial otitis. This anatomic reconstruction was accompanied by an improvement in hearing in 36 of the 39 patients in whom the ossicular chain was intact and in 5 of the 7 in whom it was broken. The results were, on the whole, less satisfactory in the cases of suppurative otitis, because suppuration threatens the vitality of the graft and favors the formation of adhesions which may interfere with any postoperative improvement in hearing. Even so, an anatomic reconstruction was obtained in 37 of the 52 patients, and the hearing was improved in 4 of 6 patients with an intact ossicular chain and in 24 of the 31 in whom the chain was broken. These results warrant the conclusion that tympanoplasty is the operation of choice in chronic suppurative otitis and its sequels.

Olfactory Sensation Stimulated by Intravenously Administered Substance. C. Semeria. Arch. ital. otol. **68**:9-78 (Dec. [Supp. 30]) 1957 (In Italian) [Milan, Italy].

The author made a psychophysiological study, which he believes to be the first recorded, of the olfactory sensation stimulated by intravenously administered substance in various groups of persons, some of them with a modal and the others with a deviant sense of smell. Threshold concentration values stimulated by intravenously administered peppermint were observed in a group of 83 persons with a modal sense of smell. In 52 (62.6%) of the subjects, the threshold of stimulation was reached by 2.5 mg. of peppermint (Mentha piperita), but on occasion quantities as high as 5 mg. or 7.5 mg. were required. Two persons did not perceive the presence of peppermint through the olfactory but only through the palatal apparatus. The mean value of threshold concentration values thus oscillated around 3 mg. of intravenously administered peppermint in 92% of the persons in this series. The thresholds were lowest at fasting state in the morning and highest at satiated state and in tired persons. The lapse of time from the moment of intravenous administration in the arm until the onset of olfactory sensation varied between a minimum of 7 to 8 seconds (in 29 persons) and a maximum of 25 seconds (in 4 persons).

Adaptation of the olfactory nerve stimulated by intravenously administered substance was observed in 39 persons with low threshold concentration values. No adaptation of the olfactory nerve was noted in 30 persons, a mild adaptation in 5, and a distinct adaptation in 4. The pupillary activity associated with the olfactory sensation was observed in 19 of 20 persons who received the intravenously administered substance. There is an immediate pupillary contraction lasting 0.5 second, followed by a mydriasis lasting from 0.5 to 1 second. The psychogalvanic reflex was observed in 14 of 16 young persons taking the test. Recordings of the olfactometric test by Elsberg showed response to intravenously administered substance in most laryngectomized persons. Threshold concentration values appeared higher in patients who had undergone laryngectomy at a more remote date than in those who had had the operation recently.

The same test was given to 322 persons with various clinical disorders; 252 of them had various types of rhinosinusal disorders, 27 had neurological disturbances, and 43 had cranial lesions. Persons with simple nasal obstruction, chronic rhinosinusal inflammations, and allergic rhinal disorders showed higher than normal threshold concentration values. There was no observed olfactory sensation stimulated by intravenously administered substance in persons with postrhinitic olfactory alterations. Inconsistent results were obtained in persons with ozena. Almost identical findings of the olfactory response to intravenously administered substance were obtained through various olfactometric procedures in persons with neurological disorders and cranial lesions.

INDUSTRIAL MEDICINE

Chronic Beryllium Poisoning. J. W. Jordan and C. S. Darke. Thorax **13**:69-73 (March) 1958 [London].

The authors describe the history of a woman who was first seen in 1955 when she was 45 years old. She had chronic cough and clubbing of the fingers. Her occupational history revealed that from June, 1943, to May, 1945, she had worked in a factory making fluorescent lamps. At the time, zinc beryl-

lium silicate phosphors in high concentration were used in the manufacture of these lamps. The patient's work consisted in placing the tubes on horizontal rollers. The solution containing beryllium was baked on the inner surface of the tubes, and after the tubes were removed from the oven, about 2 in. of deposit was extracted from each end of the tube with a rubber-padded brush. Very little dust was released, as the ends of the tube were enclosed in a box covering. Tubes were broken from time to time, and the patient received some small lacerations from these. During this period she felt quite well, and no medical or radiologic examination was made.

In 1945 the patient went to live in a small town far removed from that in which she did her factory work. A few years later a gradual deterioration in her health was noticeable, and she found that she was unable to take long walks because of shortness of breath. In 1950 an unproductive cough and vague chest pains developed, and clubbing of the fingers was first observed by the patient. During the next 5 years the cough became more severe. The patient sought medical advice, and a diagnosis of chronic beryllium poisoning was made 10 years after her last exposure. She was found to have moderate respiratory insufficiency, radiographic evidence of a diffuse granulomatous and fibrotic process in the lungs, splenomegaly, and a number of sarcoid-like granulomas on the forearm, knees, and ankles. Her skin gave a strongly positive reaction to a patch test with a dilute solution of beryllium salt. The observation that all patients with chronic beryllium poisoning show positive patch tests is thought to support the view that the development of a hypersensitive state is an essential feature in the pathogenesis of the disease.

Occupational Eczema in Shoemakers Resulting from Use of a New Type of Glue. K. E. Malten. Nederl. tijdschr. geneesk. **102**:268-272 (Feb. 8) 1958 (In Dutch) [Amsterdam].

Weeks or months after the introduction of a new type of glue, contact eczema developed on the hands and forearms of a number of shoemakers. The phenolformaldehyde synthetic resin contained in the glue was found to be the causal allergen by means of patch tests on 10 of the affected workers. The resin consisted of a catalyst of unknown composition, of formaldehyde, and of *p*-tertiary butyl phenol. Two patients had positive patch tests for formaldehyde; all 10 patients were allergic to *p*-tertiary butyl phenol, and so this was probably the primary sensitizing agent. The case histories revealed that the same or a closely related resin was a component part of various other glues. No new cases of this industrial dermatitis need occur, provided that certain precautions are taken. Preventive measures are listed.

THERAPEUTICS

Treatment of Certain Side-Effects of Morphine. G. Christie, S. Gershon, R. Gray and others. Brit. M. J. **1**:675-680 (March 22) 1958 [London].

Three drugs are necessary for the complete control of the side-effects resulting from the administration of morphine, namely, N-allylnormorphine for respiratory depression, amiphenazole for central nervous system depression (narcosis), and cyclizine hydrochloride for nausea and vomiting. Experiments and some case histories are presented to illustrate the 3 major therapeutic exhibitions of morphine: 1. Patients with incurable painful disease, in whom some degree of habituation is soon established and the incidence and severity of side-effects fall off. 2. Preoperative and postoperative patients. This group comprises a wide range of persons with respect to age and physical conditions; the postoperative group is a particularly important one, as nausea, dry retching, and vomiting can cause serious surgical sequelae. 3. Accident casualties and war-wounded in whom morphine is used as an emergency analgesic. It seemed desirable at the outset to establish the incidence and severity of the side-effects of doses of the order of 15 to 30 mg. Morphine was given by injection, usually intramuscularly but occasionally intravenously.

Summarizing their observations, the authors emphasize that the most frequent side-effects are nausea and vomiting, the incidence of which may be as high as 30%. The only really effective drug to control morphine-induced emesis is a mild antihistaminic, cyclizine hydrochloride. On the other hand, the narcotic (sedative) action of morphine is best controlled by amiphenazole. These 2 results, in man, parallel the results obtained in animals. There is also some evidence that amiphenazole can aid in the relief of morphine addiction. N-allylnormorphine would appear to be the drug of choice to restore a morphine-depressed respiratory center, although amiphenazole has some action in this regard. Morphine, in healthy people, is not the dangerous drug that has hitherto been believed. However, certain patients are susceptible to morphine. Thus, in the first series 6 out of 48 volunteers were sensitive to 10 mg. of morphine, but even in this group respiratory depression was not the major concern. It is advisable to ascertain this sensitivity by giving the conventional dose of 10 to 15 mg. If this amount is without untoward effect, then the dose of morphine should be rapidly increased to 30 mg. or more until the patient receives complete analgesia lasting 6 to 8 hours. Large doses of morphine (up to 200 mg. daily) may be required to control chronic pain. The patient should not be denied the benefit of complete analgesia on the score of side-actions or addiction. The results in over 400 cases show such fears to be groundless

when the appropriate antagonist is employed to control the particular side-action experienced by the patient.

The Effect of Repeated Increased Doses of BCG Vaccine on the Organism of Infants. A. A. Efimova. Pediatriya **36**:14-23 (Jan.) 1958 (In Russian) [Moscow].

De Assis and his co-workers in Brazil called attention to the desensitizing effect of large doses of BCG vaccine given at short intervals by the oral route. The author reports on oral vaccination of 317 children, aged from 1 month to 3 years. BCG vaccine in doses of 60 mg. was given every month for 6 doses to children who were either tuberculin negative or tuberculin positive. There were no complications, and no injurious effect upon the organism of the vaccinated child was noted. The method can be carried out along with other prophylactic vaccinations. The intensity of tuberculin allergy was observed to increase with each repeated vaccination so as to reach almost 100% at the end of the treatment. For practical purposes 2 to 3 vaccinations should suffice. Vaccination of children infected with tuberculosis is inadvisable.

PATHOLOGY

Effects of Linolenic and Stearic Acids on Cholesterol-Induced Lipoid Deposition in Human Aortic Cells in Tissue-Culture. D. D. Rutstein, E. F. Ingenito, J. M. Craig and M. Martinelli. Lancet **1**:545-552 (March 15) 1958 [London].

A chance observation led to the study of factors affecting lipid deposition in tissue cultures of cells from the human aorta. The effects of steroids, such as cortisone, on sodium and potassium exchange between the medium and human heart cells in tissue culture were under study. Cholesterol, a steroid without known direct effect on sodium and potassium exchange, was added to one of the control cultures. After 8 days' growth cells exposed to cholesterol were found to contain granules which stained with scarlet red and with Liebermann-Burchard reagents. This observation led the authors to make studies on the deposition of lipid in tissue cultures of human aortic lining in a medium containing human blood serum. Factors affecting the intracellular deposition of lipid could be investigated by this method. It was demonstrated that, when cholesterol in ethanol is added to the culture medium, the amount of lipid deposited in the cells is proportional to the amount of cholesterol added: 1. When cholesterol was added at a concentration of 1 mg. per 100 ml., there was little evidence of intracellular lipid deposition. 2. At a concentration of 3 mg. per 100 ml., intracellular lipid deposition regularly appeared and was associated with an increase in the size of the cells. 3. At a concentration of 5 mg. per 100 ml., intracellular lipid deposition was considerable, and the cells were enormously increased in size.

Similarly, when cholesterol bound to beta lipoprotein was added to the culture medium, the amount of lipid deposited in the cells was proportional to the amount of cholesterol added: 1. At a concentration of 30 mg. of added cholesterol per 100 ml., there was little evidence of intracellular lipid deposition. 2. At a concentration of 50 mg. per 100 ml., intracellular lipid deposition regularly appeared and was associated with an increase in the size of the cells. 3. At a concentration of 70 mg. per 100 ml., intracellular lipid deposition was considerable, and the cells were enormously increased in size. The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) disappeared in 5 days if the medium containing the cholesterol was replaced by a normal medium. The intracellular deposition caused by adding cholesterol (whether in ethanol or protein-bound) was completely inhibited by the simultaneous addition of linolenic acid (1 mg. per 100 ml.). It was increased by the simultaneous addition of stearic acid (1 mg. per 100 ml.). Thus, in tissue cultures of human aortic cells, deposition of lipid can be induced by cholesterol, is reversible, can be inhibited by an unsaturated fatty acid (linolenic acid), and can be potentiated by the corresponding saturated fatty acid (stearic acid).

The Natural History of Postnecrotic Cirrhosis: A Study of 221 Autopsy Cases. R. A. MacDonald and G. K. Mallory. Am. J. Med. **24**:334-357 (March) 1958 [New York].

In an attempt to study the natural history of postnecrotic cirrhosis, the authors analyzed the clinical, laboratory, and pathological features of 130 men and 91 women with this disease, whose average age was 57 years, who died, and in whom autopsies were performed at the Mallory Institute of Pathology in Boston between 1917 and 1956. Of the 221 patients, 31 had primary hepatic carcinoma in addition to postnecrotic cirrhosis, 26 had fatty nutritional (alcoholic) cirrhosis in addition to postnecrotic cirrhosis, and 164 had uncomplicated postnecrotic cirrhosis. Information related to previous hepatitis or jaundice was available from the clinical records of 190 patients, 45 (24%) of whom had had jaundice or an illness suggesting hepatitis. No evidence was found, however, that a sudden and massive liver insult had occurred in these patients. An additional 84 patients (44%) had been exposed to greater than usual risk from serum hepatitis in the course of receiving antisyphilitic and other parenteral injections in the course of previous surgical procedures. The clinical records of the patients with postnecrotic cirrhosis at autopsy, who had a history

of previous jaundice (presumably viral hepatitis), showed 2 types of clinical course after the episode of jaundice. Sixty-six per cent of these patients had been relatively well for an average period of 15 years, after which time ascites, jaundice, or right upper quadrant pain had occurred. From the time of appearance of these features the duration of life was only 2 months. The other type of clinical course was observed in about 33% of the patients, in whom the interval from jaundice to the occurrence of ascites, recurring jaundice, or right upper quadrant pain was less than 1 year, and the length of survival, once these signs appeared, averaged only 17 months.

The average duration of continuous illness before hospitalization was less than 6 months in more than 50% of the 221 patients with postnecrotic cirrhosis. Only about 20% of the patients had been continuously ill for more than 2 years. After admission to hospital the average duration of life was 22 days. The presenting complaints of the patients were chiefly ascites and edema (30%), abdominal pain (17%), and hematemesis (14%). Abdominal pain was particularly frequent among patients with hepatic carcinoma. Such features as age and sex of the patients in this study did not differ greatly from those of other patients with cirrhosis or from the general autopsy population of the Mallory Institute of Pathology. A racial difference was noted in that postnecrotic cirrhosis was relatively frequent among Chinese, although the number of Chinese patients was small. About 50% of the 221 patients had consumed alcoholic beverages to excess; the other 50% drank little or no alcohol. An adequate diet was claimed by about 66% of the patients. Poor nutrition and alcoholism were common in patients who had fatty nutritional (alcoholic) cirrhosis in addition to postnecrotic cirrhosis. Results of laboratory and liver function tests were characteristic of patients with cirrhosis, but no specific alterations for postnecrotic cirrhosis were found.

At autopsy, the liver tended to be smaller than normal, 76% of the livers weighing less than 1,500 Gm.; the color of the liver was most frequently gray to yellow, and nodules of liver tissue tended to be large and irregular, generally greater than 2 cm. in diameter, and separated by broad fibrous scars; but the occurrence of large hepatic nodules was not an invariable finding. The spleen tended to be enlarged at autopsy, with average weights between 350 and 400 Gm. A palpable spleen was not of help in determining the presence or absence of hepatic carcinoma or esophageal varices. Bloody ascites was found in 23% of the patients with hepatic carcinoma as compared with an incidence of only 2.5% among patients with uncomplicated postnecrotic cirrhosis. Esophageal varices were found at autopsy in 52% of the patients with postnecrotic cirrhosis; 50% of these showed evidence of active, recent bleeding. The principal causes of death among the patients with postnecrotic cirrhosis were infection (29%) and gastrointestinal bleeding (26%), the latter usually from esophageal varices. Gastric and duodenal ulcers were found in 9% of the patients with postnecrotic cirrhosis, compared with an incidence of 5.5% in all autopsies at this institute, a difference that is not statistically significant. However, 16% of the patients with concurrent hepatic carcinoma had peptic ulcer. Nonhepatic neoplasms were found in 27 (12%) of the 221 patients; metastases to the liver in patients with postnecrotic cirrhosis appeared to be of the same order of frequency as in patients without cirrhosis. The authors' findings in the 221 patients leave little doubt that postnecrotic cirrhosis is both clinically and anatomically a true cirrhosis.

Unsuspected Healed Myocardial Infarction in Patients Dying in a General Hospital. S. E. Gould and L. P. Cawley. A. M. A. Arch. Int. Med. **101**:524-527 (March) 1958 [Chicago].

In order to ascertain the frequency of unsuspected healed myocardial infarction, the authors reviewed a series of 5,000 consecutive autopsies and the clinical records of all patients who were found to have infarcts at autopsy. The total number of hearts with infarcts, whether old, recent, or fresh, was 588 (11.76%). The ratio of men to women with infarcts among those who came to autopsy was 1.13:1; the ratio of white to Negro patients was 2.13:1. Healed unsuspected (old, "silent") infarcts were found in 175 patients (3.5%) of all who came to autopsy and constituted 30% of all myocardial infarcts encountered at autopsy. The majority of the 175 patients with unsuspected healed infarcts (53.7%) were 70 years or older, and only 1 was less than 50 years old. Those who had congestive heart failure had associated hypertension, and particularly cardiac hypertrophy, more often than patients who did not have congestive failure. Electrocardiograms were taken in only 56 of the 175 patients with old unsuspected infarcts. In 33 the tracing was abnormal but not diagnostic of infarction.

Histological Findings in the Parametrial Lymph Nodes in Carcinoma of the Cervix. I. Priola. Minerva ginec. **9**:1017-1025 (Dec. 31) 1957 (In Italian) [Turin, Italy].

The author describes microscopic findings of the lymph nodes of the parametria excised from 37 patients with carcinoma of the cervix, on whom panhysterectomy of the Wertheim type was performed during the period from 1949 to 1950. This series of patients fell into the United Nations classifications 1 and 2. Patients with the type 2 tumor had received radium therapy before the operation.

This study revealed an early carcinomatous and metastatic invasion of the parametrial area. Presence of extensive tumor infiltration into the lymph nodes was established even in cases which could have been clinically classified as tumors of type 1. Preoperative radium therapy healed the ulcerations and reduced the parametrial infiltration, thus permitting surgical operation. Histological findings, however, revealed the existence of a considerable extent of metastases, which suggest that radium therapy was not able to reach the malignant cells seated deeply in the tissue. No signs of endometriosis and only a few degenerative lesions were seen. Tumor cells, except for the area in process of degeneration, showed structural differentiation with the characteristics of the primary carcinoma. Changes in the parenchyma of the lymph nodes were of secondary importance as compared with the metastatic process. Endothelial and follicular hyperplasias were probably defensive reactions against the tumor and its necrotic products. The high incidence of carcinoma metastases has indicated the rapidity of the progress of carcinoma of the cervix.

The opinion of the author is that irradiation could not reach the lymph nodes of the parametria. Resistance of the metastatic cells to radium therapy must be ruled out, because the original tumor had regressed when exposed to irradiation. Surgical therapy thus appears to be the best procedure for management of carcinoma of the cervix of type 1 and 2. Radium therapy is useful in preparation for the surgical operation.

A Genetic Study of Carcinoma of the Large Intestine. C. M. Woolf. Am. J. Human Genet. 10:42-47 (March) 1958 [Baltimore].

It has been established that multiple polyposis is a genetic disease, with a dominant mode of inheritance. Even though multiple polyposis is a rare disease, the occurrence of a single polyp or a few polyps (occasional discrete polyps) in the colon or the rectum is a relatively common condition, routine sigmoidoscopic examinations having shown that approximately 5% of all individuals over 35 years of age have one or more polyps in the rectum or the sigmoid. Multiple polyposis is easily distinguished from the latter condition. It is a matter of hundreds or even thousands of polyps versus one or a few. There has been evidence that even the occurrence of occasional discrete polyps may be influenced by a genetic background. Fifty-five adult members belonging to the same generation of a large Utah kindred with a high frequency of carcinoma of the large intestine were given sigmoidoscopic examination. Twenty-five were shown to have 1 or more histologically confirmed polyps. This is a much higher frequency than is expected in the general population. As a further control, 21 of the spouses of these persons were examined; only 1 had a questionable polyp, and all the others were free from polyps. Twelve to 18 months after the initial examination, more than half of the persons who had polyps at the first sigmoidoscopic examination were shown to have 1 or more new polyps, and some who had been free at the first examination now had 1 or more polyps.

Since these observations suggested that carcinoma of the large intestine could have a familial tendency due to a genetic mechanism other than that associated with multiple polyposis, a propositus study was carried out. The objective was to compare the frequency of deaths due to carcinoma of the large intestine and to other types of cancer among the relatives of individuals who died of cancer of the large intestine not associated with multiple polyposis with the frequency in a control sample. Propositi were picked from death certificates between 1931 and 1951. The names of those who died of cancer of the large intestine were traced in the genealogical archives of Salt Lake City. Family group records were available for about one-fourth of the selected names, and it was then possible to trace the death certificates of parents and siblings. The death certificates of 763 relatives of the propositi revealed 26 in whom death had been due to cancer of the large intestine, whereas only 8 such deaths were found in the relatives of controls. This difference seems the more noteworthy when it is considered that deaths from other types of cancer were practically the same in the two groups, 81 and 83 respectively. Even though the number of deaths among the relatives of the propositi is significantly greater than the number among those of the controls, it is not large enough to suggest that heredity is of greater etiological importance than some other unknown nongenetic factors. The genetic component appears to have about the same magnitude of importance as has been shown for carcinoma of the stomach and breast.

ANESTHESIA

Deaths Associated with Anaesthesia and Surgery: A Critical Analysis of 200 Cases. O. V. S. Kok. South African M. J. 32:180-186 (Feb. 15) 1958 [Cape Town].

In 1955 the South African Society of Anesthetists appointed a subcommittee to investigate deaths associated with anesthesia. The present communication is concerned with reports on the first 200 such deaths during the last 2 years. It deals only with surgical deaths referred to a district surgeon for autopsy in terms of section 86 of the Medical,

Dental, and Pharmacy Act of 1928, which is concerned "with the death of a person whilst under the influence of a general or local anesthetic, or in which the administration of an anesthetic has been a contributory cause." This report classifies deaths associated with anesthesia and surgery along the lines adopted by a committee in Great Britain, as follows: (1) deaths caused by the anesthetic agent or the technique of administration or in other ways coming entirely within the anesthetist's province; (2) similar cases, but in which there was some doubt whether the agent or the technique was entirely responsible for the fatal result; (3) cases in which the patient's death was caused by both the surgical and the anesthetic techniques; (4) deaths entirely referable to the surgical technique; (5) inevitable deaths, but in which the anesthetic and surgical techniques seemed satisfactory; (6) fortuitous deaths, e. g., those due to pulmonary embolism; and (7 and 8) cases that could not be assessed despite data or on account of inadequate data.

In the present analysis, 89 deaths (44.5%) fell into the first 3 categories (those in which the anesthetic played a major role). All age groups were represented in the 200 patients. As regards sex, there were 120 men and 80 women. The greater number of deaths in men was ascribed to a high relative incidence of serious trauma. As regards the stage of anesthesia at which death occurred, it is stated that 25 deaths occurred during induction, 88 during maintenance, 40 within 30 minutes after the operation, and 47 later. The preoperative status was good in 20 of the patients, fair in 40, poor in 84, and 56 of the patients were moribund. Cardiac arrest occurred on the operating table in 132 of the patients. Cardiac massage had been used in only 82 of the 132 patients. The author feels that the only effective treatment of cardiac arrest is immediate thoracotomy and cardiac massage, followed by defibrillation if necessary. The anesthetist must institute artificial respiration. Blind intracardiac injection of vasopressor drugs is criticized. Thiopentone (Pentothal) sodium was used for induction in 116 of 182 patients who were given general anesthesia. Of this number, 22 succumbed from primary cardiac failure. Thiopentone sodium was the most dangerous anesthetic agent. The death rate from trichloroethylene (Trilene) appears to be the highest of all the inhalation agents. There are peculiar dangers in the use of some agents for regional and topical analgesia.

The author recommends that anesthetic recovery rooms should be provided in which poor-risk patients can be nursed by experienced nurses under the eye of anesthetists and surgeons. Hospitals should also keep proper resuscitative equipment (cardiac massage drums, suction apparatus, etc.) immediately available. Departments of anesthesia should be established in all medical schools with status equal to that of other departments. Before registration as a medical practitioner, the intern should receive at least 1-month, full-time, compulsory training in anesthesiology, or he should give under supervision at least 100 anesthetics. Large hospitals should have committees to investigate anesthetic deaths. There should be compulsory notification of all deaths resulting from anesthesia, compulsory instruction in methods of cardiac resuscitation, and refresher courses for general practitioners, nurses, and other persons interested in modern methods of anesthesia.

The Effect of Hypothermia on Hemorrhagic Shock. A. T. Ferguson, J. N. Wilson, D. Jenkins and H. Swan. Ann. Surg. **147**:281-288 (March) 1958 [Philadelphia].

During the past decade many experiments were reported from which it was deduced that hypothermia has a beneficial effect on hemorrhagic shock. The authors, using different methods, were not able to corroborate this; on the contrary, there was evidence that hypothermia might impose a definite deleterious influence on the response of an animal to acute hemorrhage. In this study, 3 groups of adult splenectomized dogs were subjected to a hemorrhage of 35% of their measured blood volume. Group 1 included dogs bled in the normothermic state and served as a control. Group 2 comprised dogs that were cooled to 25 C (77 F) prior to hemorrhage. Group 3 consisted of dogs that were bled while normothermic and then cooled to 25 C (77 F). All the animals in groups 1 and 3 survived, while the animals in group 2 suffered an 80% mortality. Thus, hemorrhage in an already hypothermic dog is usually fatal, while hypothermia imposed on a dog just bled is not fatal with the bleeding volumes employed. The critical difference in the experience with these 2 groups of hypothermic animals was the existence in group 3 of a "grace period" (early cooling period) after hemorrhage, during which time compensations to the hemorrhage occurred. Hypothermia apparently altered the capacity of the dog to achieve circulatory compensation to acute hemorrhage. There was a close correlation between the blood pressure response to hemorrhage and survival. Only dogs that were bled after cooling (group 2) had a significant profound and prolonged hypotension. The value of hypothermia as a method of treatment for hemorrhagic shock is neither confirmed nor refuted by this study, but doubt is cast upon the rationale of its use. The hypothermic dog is unable to survive a hemorrhage volume which is nonfatal to the normothermic dog. Therefore, if operations are carried out under hypothermia, deficits in blood volume must be avoided.

BOOK REVIEWS

The Principles and Practice of Diathermy. By Bryan O. Scott, M.R.C.S., L.R.C.P., D.Phys.Med., Consultant in Physical Medicine, Radcliffe Infirmary, Oxford, England. Cloth. $5. Pp. 193, with 146 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1957.

Over half of this book is devoted to the basic physics and biophysics of short wave diathermy. These well-described, fundamental principles are as applicable in the United States as they are in the United Kingdom, and the use of British terminology should not trouble the American reader. The text gives scant attention to microwave diathermy, which apparently is far more widely used in the United States than in the United Kingdom. It is gratifying to note that the author clearly sets forth the medical reason for using diathermy, namely, its ability to heat tissues, and he does not contend that there are therapeutic nonthermal effects. There are good descriptions of the techniques of the medical application of short wave diathermy and appropriate recommendations as to safeguards and contraindications. There is an all-too-brief chapter on surgical diathermy. This text is recommended for use by any physician interested in diathermy. It should be of a special value in teaching the subject of short wave diathermy to medical students and physical therapy students.

Neuritis, Sensory Neuritis, Neuralgia: A Clinical Study with Review of the Literature. By Robert Wartenberg, M.D. Foreword by Wilfred Harris, M.D. Cloth. $8.50. Pp. 444, with 13 illustrations. Oxford University Press, 114 Fifth Ave., New York 11, 1958.

The late Robert Wartenberg has an established reputation as an outstanding clinician and teacher, an avid reader of the world literature of clinical neurology, a formidable critic, and a historian with tenacious devotion to the proper assignment of eponyms to signs and syndromes. These attributes are all evident in this monograph, published posthumously. The central thesis of the book is that there is a kind of neuritis which affects isolated and purely sensory nerves and which may attack different nerves over a period of many years. He describes nine cases of this type and labels the syndrome "migrant sensory neuritis." The remainder of the book is devoted to an analysis of the other major affections of peripheral nerves but relates to the central theme in an attempt to demonstrate that a general systemic disease can affect a single nerve and that either the motor or the sensory fibers in a mixed nerve may be injured. The pertinent literature is cited, and there are comments about the clinical features of such conditions as trigeminal neuralgia, sciatic neuritis, multiple cranial neuritis, and meralgia paresthetica.

The benefits to be derived from a review of the literature are illustrated in the author's critical analysis of the role of mechanical factors in sciatic syndromes and meralgia paresthetica. He clearly shows that sciatic pain is not always due to herniation of the nucleus pulposus, but this fact does not prove his statement that the involvement of the nerve is the result of a virus infection, nor is the latter thesis established by quotations from authorities, living or dead, who have expressed a similar opinion but have not presented any evidence to support their belief. Similar criticism may be directed to the author's advocacy of a viral cause for Bell's palsy, multiple sclerosis, and trigeminal neuralgia. The role of cold in the etiology of facial paralysis and sciatic pain, "abiotrophy" as a cause of atrophy of muscles innervated by the median nerve, involvement of peripheral nerves in acute poliomyelitis, a relationship between "migrant sensory neuritis" and multiple sclerosis, the dental origin of trigeminal neuralgia, and the concept of "latent neuritis" are some of the ideas advanced by the author which are not apt to meet general acceptance. Although highly speculative, the book is tersely written. It is interesting and will serve as a source of reference for syndromes of the peripheral and cranial nerves. It does not, however, provide a substitute for the description of these syndromes in the standard textbooks of neurology which are of most use to the practitioner.

Introduction to Enzymology. By Alan H. Mehler. Cloth. $10.80. Pp. 425, with illustrations. Academic Press, Inc., 111 Fifth Ave., New York 3, 1957.

The study of enzymes can properly be included as one facet in almost any book that deals with plant or animal life. It is, therefore, encountered in organic and physical chemistry, clinical medicine, plant physiology, bacteriology, biology, biochemistry, and many other sciences. Much of the investigative material in the rapidly expanding field of enzyme chemistry is somewhat isolated, and its full significance, therefore, is frequently not completely comprehended. This book is an outgrowth of a course in enzyme chemistry which the author taught to a group of investigators with varied interests. For this reason, it contains a different organization than is usually found in the many excellent monographs on enzymes that are available. The author has combined in various chapters those

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

enzymes which are involved in certain metabolic sequences, showing the interrelationships and mechanisms used and the multiplicity of factors involved in a particular sequence. Although the book is divided into nine chapters based on different metabolic sequences, enzyme chemistry is so interrelated that it is practically impossible to separate it effectively. The book contains a short introductory chapter that includes a brief history of enzyme chemistry and a short discussion of some general fundamental properties of enzymes. The metabolic sequences discussed in the following chapters include protein and peptide hydrolysis, fermentation and oxidation of metabolic fuels, the transfer of electrons, hydrogen and oxygen in biological oxidations, sugar and sugar derivatives, polynucleotides, amino acids, other acids and acid derivatives, and a final chapter on the part enzymes play in the organization of structure and function. Each chapter contains footnoted references to specific aspects of enzymes in addition to general references to the broad field under discussion at the end of the chapter. A subject index is also included.

Rand, Sweeny and Vincent's Growth and Development of the Young Child. By Marian E. Breckenridge, M.S., and Margaret Nesbitt Murphy, Ph.D. Sixth edition. Cloth. $5.50. Pp. 548, with 76 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftsbury Ave., London, W. C. 2, England, 1958.

Although this book is not strictly a medical textbook on child development, it does fill a gap in the literature by explaining some of the underlying causes of child growth and behavior. Essentially, what is presented is an attitude or philosophy that can be used in any study of children. For the paramedical cohort of the physician, this simple but scientific book provides insight into what makes the child "tick." The section on the child's physical equipment for growth, development, and functioning should be of aid to all who have to answer the worried parent's questions on a child's size and shape. The book's primary usefulness will be for students of child development, but it can also serve as a physician's reference textbook. It might be of value as a book to offer parents to confirm the physician's observations and conclusions. There is an excellent index. The style is unusually clear and concise for the material covered.

Methods in Surgical Pathology. By Henry A. Teloh, M.D., Assistant Professor of Pathology, Northwestern University Medical School, Chicago. Cloth. $4.75. Pp. 127, with 12 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

This short manual describes the fundamental maneuvers which the author has found useful, as a pathologist, in examining specimens removed at operation. Particularly valuable are the emphasis on block selection and processing, the indication of inadequacy when simple diagnostic "tagging" rather than prognosis is the result of the examination, and the need for a 24-hour schedule between operation and report. Since this is a personal production, some pathologists may find minor points of difference with various portions of the book. All would not agree with the hesitancy about the use of frozen sections on endometrium, brain, thyroid, and lymph nodes, although the admission must be made that a definite diagnosis may have to be deferred until paraffin sections are examined on this group of tissues. Despite minor criticisms, the book is a pioneer effort which fills a serious need. In the hands of a first-year resident in pathology or a clinical resident on rotation through surgical pathology, it should prove valuable in shortening the period during which he feels lost when encountering surgical specimens for the first time. There is a place for such a manual in every laboratory of surgical pathology. With minor local revisions, according to individual laboratory practices, it should prove timesaving.

Drugs of Choice 1958-1959. Walter Modell, M.D., Associate Professor of Pharmacology, Cornell University Medical College, New York, editor. Cloth. $12.75. Pp. 931, with illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

This book is a symposium of the opinions of 37 experts in therapeutics, including the editor, concerning the comparative effectiveness of drugs marketed in the United States. It is intended to serve as a practical guide to the selection of the best drug for a particular therapeutic problem, and it deals with a wide variety of purposes and situations for which drugs are generally used. Biological products have been purposely excluded, and no section on the selection of skin disinfectants was found. The subject matter comprises such topics as principles of the choice of drugs, the choice of drugs for children, the choice of a diuretic, and the choice of drugs for gastrointestinal disorders. Most of the chapters include discussions of the clinical applications and general pharmacological considerations, as well as of the classification and individual importance of the drugs involved. Selected references appear at the end of the chapters, together with a separately compiled drug index which describes various brands and dosage forms. The latter lists some drugs not mentioned in the text and some that are not generally available. A general index is also provided. Although the book is a commendable compendium of expert opinion concerning drugs of choice in today's materia medica, it is not the only source of unbiased information of this kind. Its large size makes it inconvenient for use as a practical guide. On the other hand, it should prove to be a worthwhile reference for students of medicine, clinicians, and members of allied professions who wish a comprehensive and critical treatise on the subject.

QUESTIONS AND ANSWERS

SUPPLY OF FLUIDS FOR PARENTERAL ADMINISTRATION

To the Editor:—*In a community hospital with 60 beds in medical, surgical, obstetric, and pediatric services and with a staff of 11 general practitioners and 1 surgeon, over the years the maintenance of a stock of intravenously given fluids has become confusing, due to the frequent additions of new mixtures by manufacturers. A committee is seeking information for ways of cutting down on the stock of these fluids and of still having available the required solutions for virtually all needs. Please give recommendations concerning the desirability of fructose and dextrose, whether both sugars should be included, and what electrolyte vials should be included in a full inventory.*

Michael A. McCall, M.D., Marion, N. C.

Answer.—It is not possible to give any simple rule-of-thumb answer to this inquiry. However, since fluids are frequently administered without due thought as to the reason for a particular choice, it may not be amiss to review some of the reasons for giving this form of therapy. These fluids should be given for specific purposes. The objectives of parenterally given therapy include the following considerations: (1) rehydration of cells and provision of fluid for urine formation and for insensible and other losses; (2) restoration of the volume of extracellular fluid; (3) restoration of the intravascular fluid volume; (4) supplying of calories to minimize catabolism; (5) correction of electrolyte disturbances associated with acidosis or alkalosis; and (6) prevention of deficiencies in specific electrolytes or other nutrients.

A particular parenterally given fluid is not equally effective for all purposes, although some fluids may be useful for several purposes. Usually more than one of the objectives listed above needs to be accomplished. For example, 0.45% of sodium chloride in a 5% dextrose solution can be used for rehydration of the cell, restoration of extracullular fluid, and provision of expendable fluid, as well as of some calories. However, more calories are frequently necessary than can be provided in a 5% dextrose solution without giving an excessive volume of fluid, particularly to a patient with anuria or oliguria. While acidosis and alkalosis can be combated to some extent by sodium chloride, its effectiveness depends on renal control of the relative amounts of sodium and chloride excreted, and this versatile substance does not provide for other ion deficiencies that may exist. For example, a potassium deficiency consistently accompanies an alkalosis and frequently occurs in a metabolic acidosis, particularly in the diabetic. The alkali reserve is more rapidly and effectively restored by sodium bicarbonate or lactate than by sodium chloride. The electrolyte depletion produced by chloride loss can only be adequately repaired by administration of both sodium and potassium chloride. Calories may be provided by a 10-20% dextrose solution or by invert sugar, but amino acid administration may be important if the patient is in a poor nutritional state or if prolonged dependence on parenterally given nutrition occurs. In addition, calcium administered by this method is sometimes essential, and magnesium and phosphate ions are also of importance in certain conditions. The use of invert sugar, which is half fructose and half dextrose, cannot be regarded as essential, although it may have some advantages in minimizing the tendency for hyperglycemia and glycosuria to occur from parenterally given sugar, particularly in patients with diabetes mellitus or liver diseases. It has been reported that fructose is less conducive to postinfusion hypoglycemia than dextrose, although it is not clear how frequent or important postinfusion symptoms may be in most subjects. There are several reliable commercial sources of parenterally given fluids, so that no preference need be expressed.

Answer.—It would be difficult to pick out the intravenously given fluids that would be specifically needed for a 60-bed hospital. Instead, a list of all such fluids that are used in a 300-bed general hospital follows. This hospital services all types of medical and surgical patients, and these fluids are adequate for its needs.

Alcohol (5%), in water, 1,000 cc.
Protein hydrolysate (5%), in dextrose solution, 1,000 cc.
Dextrose, thiamine, riboflavin, nicotinamide, pyridoxine, vitamin B_{12} (5%), in saline solution, 1,000 cc.
Dextrose (5%), in saline solution, 1,000 cc.
Dextrose (5%), in saline solution, 250 cc.
Dextrose (10%), in saline solution, 1,000 cc.
Dextrose (5%), in water, 1,000 cc.
Dextrose (5%), in water, 500 cc.
Dextrose (5%), in water, 250 cc.
Dextrose (10%), in water, 1,000 cc.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

Dextrose (10%), in water, 500 cc.
Dextrose (20%), in water, 500 cc.
Distilled water, 500 cc.
Invert sugar (10%), in water, 1,000 cc.
Invert sugar (10%), in saline solution, 1,000 cc.
Invert sugar (10%), potassium chloride (0.3%), in water
Invert sugar (10%), potassium chloride (0.3%), in saline solution
Invert sugar (10%), sodium, potassium, calcium, chlorine, lactate, magnesium, 1,000 cc.
Invert sugar (10%), sodium, potassium, chlorine, lactate, magnesium, phosphoric acid, 1,000 cc.
Invert sugar (10%), sodium, potassium, chlorine, ammonium, 1,000 cc.
Modified duodenal solution
Sodium chloride solution, isotonic, 1,000 cc.
Sodium chloride solution, isotonic, in 1,000-cc. pour-out bottles
Sodium chloride solution, isotonic, 250 cc.
Sodium chloride solution (5%), 1,000 cc.
Sodium chloride solution (0.45%), in water
Sodium lactate (1.87% molar solution)
Protein hydrolysate (5%), in water
Dextrose (5%), in sodium chloride solution (0.2%), 150 cc.
Dextrose (5%), w/v in sodium chloride solution (0.2%), 500 cc.
Dextrose (5%), w/v in sodium chloride solution (0.2%), 1,000 cc.

BLEEDING AND COAGULATION TESTS PRIOR TO TONSILLECTOMY

To the Editor:—*What is the latest opinion on the value and significance of preoperative coagulation and bleeding time determinations in patients requiring tonsillectomy? Is there any test that will forewarn one of a potential bleeding hazard that may exist even with a carefully done tonsillectomy and adenoidectomy?*

Robert S. Hamilton, M.D., Conrad, Mont.

To the Editor:—*The medical staff of a hospital is evaluating the necessity for routine performance of bleeding time and clotting tests preliminary to tonsillectomy and adenoidectomy. Please give information as to whether these tests are currently required as legal "common usage" or have been generally discontinued as being not significant.*

Robert C. Olson, M.D., Menominee, Mich.

Answer.—Most large clinical groups have abandoned routine determinations of coagulation and bleeding times among patients who are to undergo tonsillectomy. This has been done because so few instances of a bleeding abnormality were ever found without an accompanying history or physical finding of a hemorrhagic diathesis. The most important safeguard before tonsillectomy is performed is the obtaining of a satisfactory history from the patient or the patient's family. Any patient who has a history of easy bruising or a tendency toward bleeding should have a more thorough examination of his coagulation mechanism than simply determination of the coagulation and bleeding times. Determination of the bleeding time might detect pseudohemophilia or possibly unrecognized thrombocytopenic purpura, but it is rather unlikely that it would do so in the absence of an adequate history, which should serve as a warning. Determination of the coagulation time would not bring to light anything but hemophilia that happened to be active at the moment, and, even so, it is not uncommon to find patients with hemophilia in a relatively quiescent state who present a normal coagulation time. A definite history of bleeding in these patients would be most helpful, since mild hemophilia commonly creates much difficulty at the time of operation. Also, determination of the coagulation time might fail to detect a deficiency of prothrombin, as well as lack of some of the other coagulation factors. For these reasons it would seem best to direct questions toward antecedent bruising or bleeding, and, if such a history is obtained, a more thorough study of coagulation factors, as well as the platelet count, should be carried out. If no such history is obtained, it would be relatively safe to proceed with tonsillectomy.

Answer.—Routine coagulation and bleeding time determinations prior to tonsillectomy are valueless. Most of the determinations are done either in glass tubes or in glass capillaries. Frequently, the coagulation time, as determined by these methods, shows normal values even in cases of hemophilia. The best "test" is to question the patient carefully as to hemorrhagic disturbances, both in himself and in his family. The only tests that would actually forewarn one regarding a hemorrhagic disturbance would involve a complete hemorrhagic survey, which is unjustified for a minor operation. Under the circumstances, the best thing to do is to question the patient carefully and then have hemorrhagic tests done only in doubtful cases.

Answer.—For many years, many competent throat specialists have questioned the value of coagulation and bleeding time determinations as a routine measure. Instead, reliance has been placed primarily on a history of bleeding in the patient and the patient's family. A positive history should be followed by comprehensive physical and blood examinations, including coagulation and bleeding time determinations.

Answer.—At best, coagulation and bleeding time determinations performed preoperatively in persons requiring tonsillectomy and adenoidectomy are crude clinical procedures. In general, the slide method test for coagulability may be disregarded if findings show the time prolonged to no more than two or three times that accepted as normal. However, if results show an unusually prolonged time, the patient should have comprehensive physical and blood examinations.

SCREENING FOR DIABETES

To the Editor:—*Please comment on the following procedure to detect diabetes: First, a 24-hour urine specimen is examined for sugar and a blood sugar test is done one and one-half to two hours after a meal. If findings in the first test are positive and/or the blood sugar level is over 120 mg. %, a glucose tolerance test is done. If any one specimen in the glucose tolerance test has a level of over 160 mg. % and/or the blood sugar level does not return to the original value or normal after two hours, the patient is considered to have an abnormal or potentially diabetic curve. These are strict criteria, thus eliminating steroid provocation tests.* *M.D., Maine.*

Answer.—Any screening procedure runs the risk of two opposite errors: (1) true cases of disease are missed, and (2) normal persons are falsely labeled as having the disease. Assuming that the method of determining blood sugar level referred to is that of Folin and Wu, which gives normal values of 80 to 120 mg. per 100 ml., the procedure outlined is sound in that it will rarely miss a case of true diabetes. Parenthetically, a postprandial blood sugar value much greater than 120 mg. per 100 ml.—say, 180 or higher—is diagnostic of diabetes, and a glucose tolerance test is not required. At the same time, the strict criteria that largely exclude false-negative results are apt to include some false-positive findings, that is, persons with such conditions as hyperthyroidism, gastrointestinal anastomoses, or starvation may be labeled diabetic when they are not. The inquirer recognizes this possibility when he refers to "abnormal or potentially diabetic" curves. The validity of borderline glucose tolerance curves for the diagnosis of diabetes must be determined by the exclusion of other conditions and, frequently, by further testing.

HEATING AND MULTIPLE SCLEROSIS

To the Editor:—*A 30-year-old woman has had multiple sclerosis for the past three years. Physiotherapy (such as hot baths) seems to help her most during troubled periods. She now plans to build a house and is concerned with what type of heating system to install. She appreciates that hot baths are good, but are there any real suggestions in favor of wall heat versus forced draft, steam, or solar heat?*

M. C. Florine, M.D., Janesville, Minn.

Answer.—The question brings up two considerations: 1. What, if anything, is there in heating that may influence the course of multiple sclerosis? 2. If there is a relationship, which type of heating would be most favorable? In answer to the first question, there is uniform agreement that chilling and infection, e. g., colds and sinusitis, are often events associated with a relapse. The second consideration, therefore, boils down to the choice of a system most likely to give heating throughout the house with minimum variation in temperature, minimal air movement or "drafts," and least drying effect on the mucous membranes because of low relative humidity. Though such considerations are largely empirical, most physicians would agree that these three environmental conditions do appear to play a role in the pathogenesis of acute upper respiratory infections. One may immediately eliminate solar heat as not pertinent to the discussion, since it refers to a choice of a source of energy for heating rather than to the type of heating system. Further, when this is used some kind of auxiliary conventional system is necessary. Steam heat is efficient, but, because the radiators present a large, exposed surface area at a high temperature, hot air currents are induced by convection. This effect is regarded as helping produce irregular temperature levels in the room and excessive drying of the mucous membranes. The same may be said for hot water heat, though to a lesser extent since the temperature of the radiators would be lower. Forced draft eliminates high temperature surfaces and drying, but the system must be carefully designed to avoid drafts. Radiant heat, attained by placing hot water pipes in floor, ceiling, or walls, is probably the best solution for uniform and healthful conditions. One may raise the point of living in a year-round warm climate. Although such an environment may appear to be desirable from the point of view of respiratory infections, it should never be considered if the move will raise economic and emotional problems.

POSITIVE FINDINGS IN HINTON SEROLOGIC TEST

To the Editor:—*A 26-year-old man, about to be married, showed positive findings in a Hinton serologic test. He was given a course of therapy with sterile procaine penicillin G with aluminum stearate suspension, 1 million units for 10 consecutive days. One month later, another Hinton test showed positive findings. How can the case be controlled and the patient cured? What is the latest treatment? Is a spinal fluid test advised? The patient did not contract any foreign diseases, and he does not remember any initial sore anywhere.*

S. B. Kaufman, M.D., Fall River, Mass.

Answer.—Apparently the serum of this patient was not titrated for units. It should be titrated despite the fact that he has had penicillin treatment; a low titer makes one suspicious of a false-positive serologic test. If a patient gives no history of having contracted syphilis and bears no physical or neurological signs to support such a diagnosis, one should always be suspicious of a false-positive serologic test. A Treponema immobilization (TPI) or some of its variants should be performed and re-

checked. If findings in the TPI test are negative, then the patient does not have syphilis (98% accurate). If findings in the TPI test are positive, the patient does have syphilis. He should then have a complete physical and serologic examination, including examination of eyegrounds, roentgenogram of the chest to exclude cardiac and aortic changes, and spinal fluid examination to exclude central nervous system syphilis. In the event that findings in the TPI test are positive and those in all of the other tests, including the spinal fluid examination, are negative, then the patient should have at least two more courses of therapy with penicillin, 10 million to 12 million units given in doses of 1 million units each and repeated again after three months (long-acting penicillin given twice a week). The serum should be titrated three months after each course of treatment. If findings in the TPI test are negative, it means that this man may be, at the present time, suffering from one of the hidden collagen diseases. At least 25% of such persons have been known to develop such diseases. Also, it is possible that he may have contracted malaria or some other infectious disease which could be responsible for the false-positive serologic test.

SERUM CHOLINESTERASE AND MYASTHENIA GRAVIS

To the Editor:—*A patient who has proved myasthenia gravis at present is taking neostigmine and doing fairly well; however, in the course of his illness he suffered a cerebral thrombosis, and a laboratory examination was done. Because he had worked in greenhouses all his life and had been in contact with numerous and varied insecticides, a serum cholinesterase determination was made. The level was abnormally low and has been repeatedly so. Is there any information available regarding cholinesterase levels in patients with myasthenia gravis?*

John M. Gunsolus, M.D., Stuart, Fla.

Answer.—Serum cholinesterase determinations have been reported in patients with myasthenia gravis since 1939. The first reports in the literature stated that levels of untreated patients were higher than normal and that such drugs as neostigmine, when injected, would reduce them to normal or below normal ranges. A number of more carefully worked out determinations, in which the level of cholinesterase in the red blood cells was determined as well as that in the serum, showed that the resting levels of patients with myasthenia gravis who were not under treatment were within normal ranges. It has been agreed essentially that injection of an anticholinesterase, such as neostigmine, will reduce the serum cholinesterase level slightly, and, in overdosage of this medicine, in either normal persons or patients with myasthenia, lower levels will be encountered. Such substances as the alkyl phosphates, when taken in excess, will result in very low serum cholinesterase levels, and this will persist for some weeks or months. In the case reported, since the patient is taking neostigmine, one would expect that the cholinesterase level might be normal or slightly low. This consultant has no evidence that chronic residuals from insecticides affect the level of serum cholinesterase.

AMENORRHEA AND ABDOMINAL MASS

To the Editor:—*A 15-year-old girl has amenorrhea of four months' duration but no other symptoms of consequence. Her catamenia started at 12 years of age and was regular every 29 days until four months ago. Physical examination is essentially normal, except for slight obesity and, on rectal examination only (because of the intact hymen), a cystic mass which was felt in the right adnexa. It was about 7 by 7 by 6 cm., freely movable, and painless. The patient was reexamined two weeks later, and the same mass was palpated. A roentgenogram of the abdomen and an intravenous pyelogram were done, and findings were reported by the radiologist as negative. Should dilation and curettage be done while the patient is being examined under anesthesia prior to laparotomy for the cyst?* *M.D., Florida.*

Answer.—Before examination under anesthesia is done, pregnancy tests are suggested. A uterine probe would help to determine whether the mass is uterine or adnexal. If it is adnexal, laparotomy should be done, and if it is uterine, waiting another month for observation would enhance the chance of making an accurate diagnosis both by x-ray and bimanual examination. If the diagnosis is still uncertain, then dilation and curettage would be indicated and future treatment predicated on the findings.

MONOZYGOTIC OR DIZYGOTIC TWINS

To the Editor:—*A woman whose blood group is O, Rh negative, and subtype cde/c has male twins with blood group O, Rh positive, and subtype CDe/c. The mother has congenital coloboma of the irises, and one of the twins has this same anomaly. The pathologist's report on the placenta is twin fused placenta with double sacs which have a double wall. There are two cords. Is it possible on the basis of this information to state definitely that these are single or double ovum twins?* *Robert R. Livingston, M.D. Glenwood Springs, Colo.*

Answer.—The Rh information in this question is not helpful in determining whether the twins in question are from a single ovum or a double ovum. Nesbitt (Perinatal Loss in Modern Obstetrics, London, H. K. Lewis & Co., 1957) has recently stated, "The ability to determine the origin of twins from

the relations between the placenta and its membranes has been questioned in recent years.... The placenta and membrane relations will, in most instances, however, show whether the twins are from one or two eggs. The one fallacy in this method is that at least 20% of monozygotic twins are not monochorial but are dichorial, and therefore at least 10% of all dichorial placentae do not belong to dizygotic but to monozygotic pairs.... Contrariwise, however, all monochorial placentae belong to monozygotic pairs." One could conclude, therefore, that the twins referred to in this question are not identical twins from two ova, although there is about a 10% chance that they are identical twins from the same ovum.

PAINTING DURING PREGNANCY

To the Editor:—*There is a prevalent belief that pregnant women should not paint or in any way expose themselves to paint fumes, because the turpentine in paint fumes might cause abortion. Is there any basis in fact for such precautions? If so, would the use of paints containing no turpentine be permissible?*

Melvin A. Marousek, M.D., Belle Fourche, S. D.

Answer.—There is no basis for the belief that the paint which is available today and used either for art or for ordinary decorative purposes, such as painting furniture or closets, will cause an abortion.

CARPE BOSSU DISEASE

To the Editor:—*What is the condition known as Carpe Bossu disease?* *M.D., Connecticut.*

Answer.—The condition called Carpe Bossu disease is one in which there is a ninth carpal bone, referred to as the carpal styloid bone, at the base of the third metacarpal. It may become quite painful and be associated with tenderness and swelling. The condition should be coded as 233-031.x Supernumary carpal bone with disturbance of function.

ALLERGY TO MUSHROOMS

To the Editor:—*Regarding hypersensitivity to mushrooms, a question on which appeared in the Questions and Answers section of* The Journal, *March 8, 1958, page 1262, it is important to point out that it is a common fallacy today that gastrointestinal disturbances to a food imply allergy to the inciting substance. Although the relationship of symptoms to ingestion of mushrooms in the case cited would seem to be unquestionable, it would be valuable to know whether the patient really had an allergy. The reaction might well be one of nonimmunological intolerance. There are many nonspecific irritant or toxic principles in mushrooms in small concentration, to which reactions comparable to that of favism to the pollen or beans of Vicia fava may occur. These affect only a few individuals predisposed to react to these small amounts. Further, the drying or dehydrating which renders a food nonallergenic (Fries and Glazer,* J. Allergy **21:** *169, 1950) usually destroys naturally contained irritants as well. Positive findings in skin tests for gastrointestinal disorders are rarely obtained, although in this instance of such severe symptomatology they might be seen. For reasons of safety, scratch tests should be done first, and only later the more sensitive intracutaneous tests should be made. As the consultant has implied, desensitization through the parenteral route is hazardous and through the oral route ineffective. The patient should learn to avoid gravies and dressings.*

Joseph Harman Fries, M.D.
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The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The statement that heating and drying of a food distinctly lessens its antigenicity is quite right. Fresh bananas and extracts of fresh bananas can constitute potent allergens and can cause anaphylactic shock, as well as urticaria and gastrointestinal symptoms. Other foods, too, e. g., milk and eggs, are also less allergenic when they are heated and/or dried. Nevertheless, mushooms are a form of yeast and can be potent allergens, and, in the patient under consideration, fresh mushrooms always led to severe reactions—dried mushrooms did not. If this phenomenon is an allergic one, and this consultant is convinced it is, the patient should be allergic and should show this by a positive scratch test for mushroom extract; if the scratch test is negative, an intradermal test should be done (1:1,000). In addition, the patient should exhibit other evidences of allergy, e. g., family inheritance, blood eosinophilia, or other allergies. If findings in all these tests prove negative, then and only then would this consultant believe that the symptoms could have a nonallergic basis. Mushrooms are readily eaten by almost all people; they are not in the same class as peppers and other spices. Coca and associates (Hypersensitiveness, Anaphylaxis, Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1931, p. 438) make this comment: "Mushrooms are used fresh, canned, dried, and powdered. They are useful for flavoring soup, beef tea, and a number of other foods. The juice pressed from mushrooms, seasoned with spices, is employed in the preparation of catsup to be used as such or as a base for other sauces."*